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EXPERIMENTAL AMYLOIDOSIS IN MICE*

EFFECT OF DIFFERENT FORMS OF DIET

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CHICAGO

In a preceding paper¹ the attempt has been made to explain the amyloid degeneration that occurs in white mice after from forty to sixty injections of foreign proteins on the base of an acquired hypersensitivity against the injected substances. The following facts warrant this explanation: The onset and the development of the degenerative changes depend mainly on the number of injections. The amount of the single injection is not essential, nor is it the kind of protein that is being used. In recent experiments typical amyloidosis has been produced by means of crystallized egg albumin. In the sensitized organism the reinjected protein causes an abnormal cleavage of body tissue. Cleavage of body tissue for a long time has been known to be the principal cause of amyloidosis. Observations made by Letterer and published since the first paper went to press, support this explanation. Letterer² described amyloidosis in mice following the implantation into the peritoneal cavity of sterile pieces of spleen, liver, kidney and heart obtained from mice. He concludes that the resorption of substances liberated from the implanted tissue that becomes necrotic leads to destruction of body proteins. The toxic effect of sterile autolysis in vivo has also been shown by Mason and Davidson.³

Objections to the possibility of producing amyloidosis by injecting nutrose have recently been made. While Strasser⁴ and Smetana⁵ fully confirmed Kuczynski's⁶ observations on amyloid, Ushino,⁷ a pupil of Aschoff, was less successful. He emphasizes bacterial contamination.

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1. Jaffé: Amyloidosis Produced by Injections of Proteins, Arch. Path. **1**:25 (Jan.) 1926.

2. Letterer: Verhandl. d. deutsch. path. Gesellsch. **20**:301, 1925.

3. Mason and Davidson: J. Lab. & Clin. Med. **10**:622 and 997, 1925.

4. Strasser: Ztschr. f. d. ges. exper. Med. **36**:381, 1923.

5. Smetana: Bull. Johns Hopkins Hosp. **37**:383, 1925.

6. Kuczynski: Klin. Wchnschr. **2**:722 and 2193, 1923.

7. Ushino: Verhandl. d. deutsch. path. Gesellsch. **20**:304, 1925.

This, however, could be excluded in our experiments, since cultures made from the muscles into which the injections had been made remained sterile. Ushino discusses also the possibility that the injections into the muscles may cause necrosis and that the resorption of this necrotic tissue may lead to amyloidosis. This question could easily be tested. Six mice received daily injections with 0.5 cc. of sterile saline solution. They were killed after the seventieth injection; none showed amyloid. From these experiments another conclusion can be drawn, namely, that the insignificant amount of killed bacteria or of bacteria products probably present in the salt solution used to dissolve the proteins can be neglected. A spontaneous amyloidosis in apparently normal mice, as mentioned by Wells,⁸ was not observed. One control developed a spontaneous epithelioma of the ear, and two others had abscesses in the abdominal wall. They were the only controls that showed amyloid.

A survey of the literature on experimental amyloidosis reveals that no attempt so far has been made to prevent it. Doederlein, Klinge and Wacker⁹ recorded that painting white mice with coal tar frequently causes amyloidosis. If, however, the mice were fed cholesterol and fat, they usually remained free from amyloid (Klinge and Wacker). On the other hand, a diet rich in proteins is said to cause amyloidosis (Kuczynsky, Smetana). Smetana used Swiss cheese and Kuczynsky cheese and egg albumin, but they did not investigate whether other forms of protein diet may have a similar effect.

A study of the question whether lipoids may influence the formation of amyloid is suggested through the observations of Jobling and Petersen¹⁰ and of Pfeiffer.¹¹ These investigators found a certain protective action of lipoids in intoxications associated with an abnormal cleavage of body proteins.

The mice subjected to the protein injections were fed fat diets of different composition. Injections of lipoids were not used, because the total number of injections would have been too great. After having learned of Klinge's and Wacker's findings, cholesterol was added to the fat mixtures. A group of mice was kept on a diet rich in proteins while the control mice were fed the standard diet consisting of white bread, oats and skimmed milk diluted with equal amounts of tap water.

METHODS

The fat diet consisted of 12 Gm. wheat flour, 60 Gm. skimmed milk diluted with equal parts of tap water, 6 Gm. lard, 3 Gm. fresh butter, and 0.5 Gm. cholesterol. The cholesterol was ground up with the lard and butter. The whole

8. Wells: *Chemical Pathology*, ed. 5, Philadelphia, W. B. Saunders Company, 1925, p. 472.

9. Doederlein, in Klinge and Wacker: *Krankheitsforschung* 1:257, 1925.

10. Jobling and Petersen: *Ztschr. f. Immunitätsf.* 24:219 and 292, 1916.

11. Pfeiffer: *Krankheitsforschung* 1:407, 1925.

mixture formed a paste which the mice ate eagerly. Each mouse received daily 3 or 4 Gm. of the paste containing about 20 mg. of cholesterol. Every sixth day plain diet was given. Fresh tap water was supplied ad libitum. The mice of the protein group received dried beef heart powder. The powder was moistened with tap water, and a dough was made with the aid of a little yeast. The daily ration was 2 or 3 Gm. and tap water. This diet was also taken very well, and the trays on the next morning were always empty. Once a week stock diet was given.

The mice were kept in separate cages. After having become accustomed to the new diet, they received daily injections with 0.5 cc. of a 3 per cent nutrose solution. Four mice of each group did not receive injections and served as controls.

It was found that the formation of extensive general amyloidosis could be hastened by preparing the nutrose solution in a different way than that described in the first paper. The nutrose was dissolved in saline solution at 50 C. and immersed in boiling water for fifteen minutes. Using this solution, general amyloidosis was constant after fifty injections.

A series of mice first received the nutrose injections, and they were put on fat diet after the seventeenth, twenty-ninth, thirtieth and thirty-second injection, the injections being continued.

The first animals were killed after the fifty-fifth injection. At this time amyloidosis in 100 per cent of the controls on plain diet was found. The mice were anesthetized with ether, and the heart was exposed by an incision through the sternum. Blood was drawn with the aid of a tuberculin syringe and allowed to run into a graduated centrifuge tube containing 30 mg. of lithium oxalate. Blood sufficient for the determination of the nonprotein nitrogen (Folin and Wu's method) and of the cholesterol (Bloor's second method) was usually secured; 0.5 cc. of blood was used for the nitrogen determination and 0.6 cc. for the cholesterol. After precipitating the proteins, and after extracting the lipins for two hours at 50 C., the tubes were centrifuged at high speed, and the perfectly clear and colorless supernatant fluid was used.

The time between death and the last injection was twenty-four hours; that between death and the last feeding twelve hours. In a special group referred to below, the time between feeding and death was two, three and four hours.

CHOLESTEROL FAT DIET

Cholesterol Metabolism of the Normal Mouse.—Feeding the omnivorous mouse cholesterol (dissolved in a sufficient amount of fat in order to secure optimal resorption in the intestine) does not produce the hypercholesterinemia that is typical of the herbivores, especially the rabbit (table 1). There is only a slight transient rise of the blood cholesterol following the meals. After the animals became accustomed to this diet, no increase of the cholesterol of the blood at any time was noted. According to the current view, it is the quick elimination of the cholesterol through the liver that prevents its accumulation in the blood of the omnivores. This quick elimination also accounts for the fact that the reticulo-endothelial cells of the mouse do not store the cholesterol.

The mice on cholesterol fat diet show a marked increase of the subcutaneous fat tissue and compact layers of fat tissue about the kidneys and the sex organs.

Of the internal organs, the liver takes part in the storage of the fat (fig. 1). The liver of the mouse normally plays an important rôle in the fat metabolism, and the liver cells during digestion always contain fat droplets (Wolff¹²). The fat content is much greater and persists much longer when cholesterol fat diets are given. The fat takes a different form, namely, the droplets are much larger and more or less completely fill the cells. When tested between crossed Nicols many double refracting crystals are found. The epithelial cells of the bile ducts remain free from fat; so do the Kupffer cells, which reveal signs of proliferation such as many mitotic figures and formation of intracapillary nodules.

TABLE 1.—Results of Chemical Examination of Blood

| Group | Cholesterol | | Nonprotein Nitrogen | |
|--------------------------|-------------|---------|---------------------|--------|
| | Average | Range | Average | Range |
| Normal controls..... | 185 | 120-151 | 27 | 20-35 |
| Fat controls..... | 134 | 112-151 | 28 | 22-32 |
| Fat nutrose..... | 137 | 131-144 | 37 | 33-42 |
| Beef heart controls..... | 136 | 120-146 | 60 | 39-77 |
| Beef heart nutrose..... | 125 | 110-156 | 83 | 46-184 |
| Nutrose controls..... | 123 | 116-130 | 54 | 39-77 |

The histologic examination of the small intestine at the height of digestion shows the well-known pictures of fat resorption through and between the epithelial cells. The stroma of the villi is filled with single and double refracting lipid droplets of different size and shape. Much optically active fat is found in the central lymph space. The finest fat granules are observed in the blood capillaries underneath the epithelium, which are greatly distended during digestion. The droplets stand out distinctly between and about the red blood corpuscles. Great care was taken to avoid an artificial squeezing of fat into the capillaries. The pieces before sectioning were rinsed with saline solution and were cut in the direction from the muscularis toward the internal surface.

The fat granules were present only in the subepithelial capillaries. They seemed to disappear toward the center of the villi, and no fat was found in the central vein nor in the veins of the submucosa. It appears that the fat, after having entered the blood stream, changes into an invisible form.

The possibility of fat absorption through channels other than the lymphatics has been suggested also by the chemical studies of Bloor,¹³

12. Wolff: Virchows Arch. f. path. Anat. **252**:297, 1924.

13. Bloor: J. Biol. Chem. **23**:317, 1915.

D'Errico,¹⁴ Eckstein,¹⁵ Hamburger,¹⁶ Hall,¹⁷ Joannovicz and Pick¹⁸ and Munk and Friedländer.¹⁹

No changes in other organs resulted from the peculiar diet. In the beginning of the fat diet, lipoid granules in the epithelial cells of the tubuli contorti were found. They disappeared later. No increase of fat in the cortex of the suprarenals could be found. Schmidt²⁰ mentioned that double refracting fat usually appears in the cortex of the suprarenals of cholesterol fed mice. But the cortex of the suprarenals of the mouse normally contains varying amounts of microscopically visible cholesterol compounds, and this often to the same extent as after feeding cholesterol. The same is to be said about the sweat glands. The size of the component cells and the amount of anisotropic fat globules in the cells are not greater after cholesterol diet than they are before. The fatty layer covering the epidermis is of the same thickness in both controls and cholesterol mice. In the lungs, a larger amount of fat-carrying cells was sometimes found in the alveolar septums. The fat was not double refracting.

Cholesterol Fat Diet and Nutrose Injections.—The diet rich in cholesterol and fat increases the resistance of the mouse against the harmful effect of long continued intramuscular injections of foreign proteins. While the mice on plain diet develop extensive amyloidosis after from forty to fifty injections, the animals fed the cholesterol paste after seventy injections are still free (tables 2 and 3). The protecting action of the lipins is but a relative one, for even the cholesterol mice show amyloid degeneration after more than seventy-five injections. The changes, however, are less extensive than they are in the controls. None of the mice of the cholesterol group died spontaneously, whereas 30 per cent of the controls died between the thirtieth and sixtieth injection.

Feeding cholesterol and fat when started after the animals have been sensitized does not protect (table 2).

The influence of the cholesterol fat diet on the changes stipulated by the nutrose injections is also evident from the behavior of the non-protein nitrogen of the blood (table 1).

The nonprotein nitrogen after from thirty to forty injections of nutrose into mice on plain diet is found to be constantly higher than normal. Sometimes the increase is only slight; sometimes it is more than three times normal. This increase appears later when fat diet is

14. D'Errico: Arch. di fisiol. **4**:513, 1907.

15. Eckstein: J. Biol. Chem. **62**:737, 1925.

16. Hamburger, in Eckstein (footnote 15).

17. Hall: Ztschr. f. Biol. **62**:1923.

18. Joannovicz and Pick: Verhandl. d. deutsch. path. Gesellsch., 1910.

19. Munk and Friedländer, in Eckstein (footnote 15).

20. Schmidt: Virchows Arch. f. path. Anat. **253**:432, 1924.

given. For example, the nonprotein nitrogen of a mouse that was kept on plain diet and showed advanced amyloidosis after fifty-three injections was 76 mg. per hundred cubic centimeters of blood. A cholesterol mouse with seventy injections and still free from amyloid gave 32 mg., and another mouse with eighty-five injections and mild general amyloidosis 42 mg.

The injections of nutrose at first do not affect the storage of fat in the physiologic fat deposits and the accumulation of lipins in the liver. Thus, the liver cells after from fifty to sixty-five injections still are filled with droplets of neutral fat and double refracting spherocrystals (fig. 2).

TABLE 2.—*Fat Diet*

| Days on Diet | Number of In- jections | Amyloid in | | | | |
|--------------------|------------------------------|------------|-------|--------|------------|-----------|
| | | Spleen | Liver | Kidney | Suprarenal | Intestine |
| 63 | 55 | 0 | 0 | 0 | 0 | 0 |
| 71 | 60 | 0 | 0 | 0 | 0 | 0 |
| 78 | 65 | 0 | 0 | 0 | 0 | 0 |
| 82 | 68 | 0 | 0 | 0 | 0 | 0 |
| 85 | 70 | 0 | 0 | 0 | 0 | 0 |
| 96 | 78 | Trace | 0 | 0 | 0 | 0 |
| 102 | 85 | ++ | + | Trace | + | Trace |
| 20 | 52 | +++ | ++ | + | ++ | + |
| 26 | 55 | ++ | ++ | + | + | + |
| 30 | 60 | +++ | ++ | + | + | + |
| 48 | 65 | +++ | ++ | ++ | + | + |

TABLE 3.—*Plain Diet*

| Number of Injections | Amyloid in | | | | |
|----------------------------|------------|-------|--------|------------|-----------|
| | Spleen | Liver | Kidney | Suprarenal | Intestine |
| 30 | +++ | +++ | ++ | ++ | + |
| 37 | +++ | +++ | ++ | + | + |
| 53 | +++ | ++ | +++ | ++ | + |
| 66 | +++ | ++ | + | + | + |

Antedating the amyloid degeneration for a short time, the fat starts to disappear from the physiologic deposits and from the liver cells. The difference between the microscopic fat content of the liver after the fifty-sixth and the eighty-fifth injection is striking. After fifty-six injections, the liver cells contain just as much fat as they do in the cholesterol fed controls. After eighty-five injections, most of the fat is gone (fig. 3). Although some fat still is present, it is of a different character and morphology. The droplets are small. They give no or little double refraction (fig. 4). The fatty changes are associated with signs of cellular disintegration such as vacuolization or hyalinization of the cytoplasm and swelling and pyknosis of the nuclei. No changes of the nuclei of the liver cells apart from the mechanical deformation are observed as long as the cells are filled with stored fat.²¹

21. The cholesterol content of the suprarenal cortex is not influenced by the nutrose injections. Even when amyloid is found in the zona reticularis, the cells of the fasciculata are filled with single and double refracting fat droplets.



Fig. 1.—Liver of a mouse which was kept on cholesterol fat diet for ninety-nine days; liver cells are crowded with fat droplets. Note single very large fat drops; no fat in Kupffer cells. Ten per cent liquor formaldehydi, sudan III, hematoxylin.

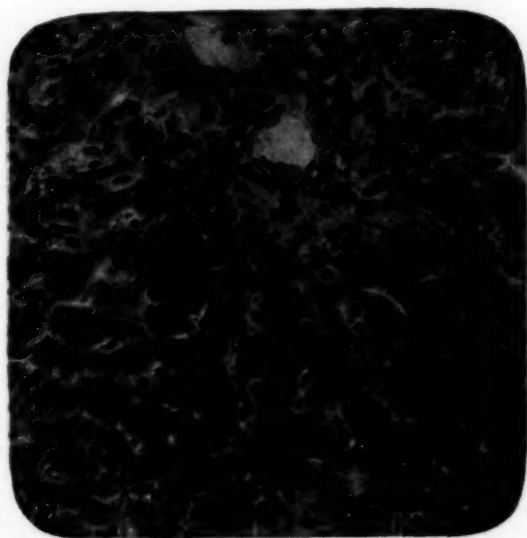


Fig. 3.—Liver of mouse kept on cholesterol fat diet for one hundred and two days and receiving eighty-five injections of nutrose. Liver cells contain very little fat; many are free from it. Pyknosis of nuclei in some cells. Small lipoid granules in the Kupffer cells. Beginning pericapillary amyloidosis. Ten per cent liquor formaldehydi, sudan III, hematoxylin.



The accumulation of fat in the liver cells is also greatly impaired when the cholesterol fat feeding is started after the twentieth injection. At no time, even not as early as after thirty-five injections, do the liver cells contain larger amounts of lipoids.

One may suggest that the sick mouse does not take sufficient food in order to secure a visible fat storage in the liver. But the mice with beginning amyloidosis eat the fat paste just as well as do the normal mice, and when killed during digestion the villi of their small intestine are crowded with fat droplets.

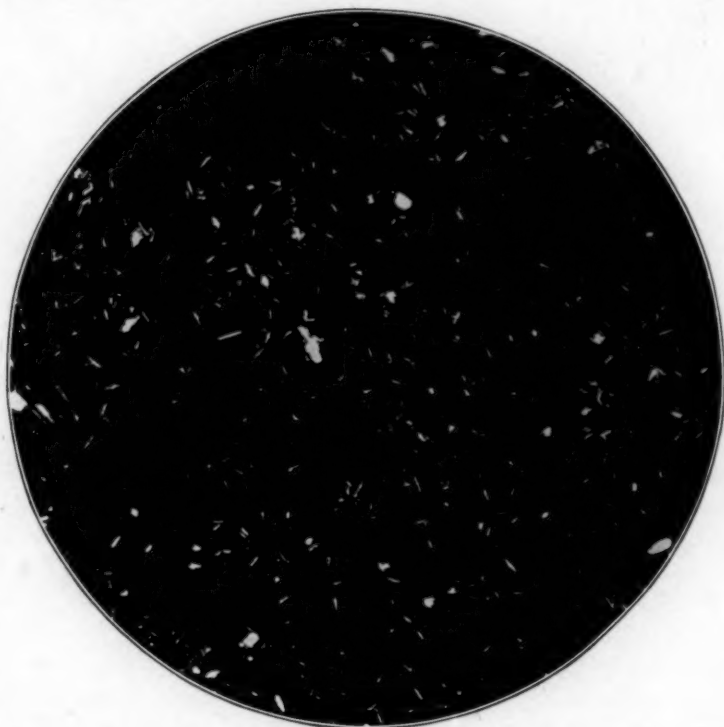


Fig. 2.—Liver of mouse kept on cholesterol fat diet for seventy-one days that had received sixty nutrose injections. Many double refracting crystals of cholesterol esters in the liver cells. Ten per cent liquor formaldehydi; unstained frozen section.

The marked decrease of the cholesterol stored in the liver cells of the mice fed this lipin that occurs after very long-continued nutrose injections is not associated with a persistent rise of the cholesterol in the blood. Only when the mice are killed from three to four hours after the feeding is there a distinct rise of the blood cholesterol. It then amounts to 180 mg. and more; but from ten to twelve hours later it is again normal. The elimination of the cholesterol is apparently delayed but not completely impaired.

The Fat Content of Amyloid.—The amyloid produced experimentally in animals as well as that of human beings contains varying amounts of fat microscopically demonstrable with the aid of fat stains, such as sudan III and Nile-blue sulphate. The fat either appears as small droplets or as finest dustlike granules. Sometimes the amyloid is found free from fat. In the liver, much fat is found in the amyloid about the portal capillaries, while it is scanty in or absent from the amyloid in the wall of the larger vessels. Kuczynski, in accordance with his conception of the origin of the amyloid, assumes the fat to be precipi-

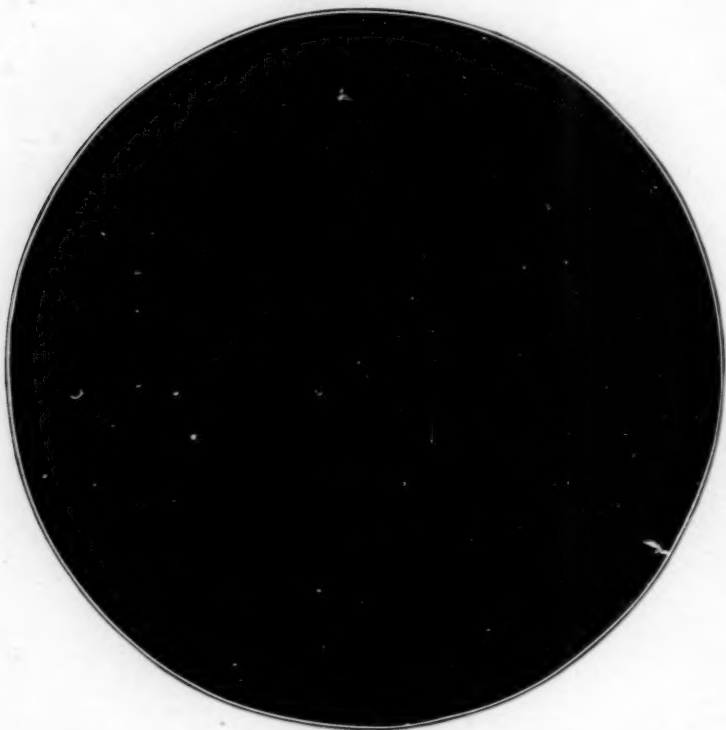


Fig. 4.—Same as figure 3. Very few and small double refracting crystals as compared to figure 2. Ten per cent liquor formaldehydi; unstained frozen section.

tated out of the tissue fluids by the coagulating amyloid. This explanation does not take into consideration the fact that in the same microscopic field the amyloid in some places may be full of fat droplets, while in others it may be free from fat. This holds true for both human and animal amyloid.

Comparing the different stages of amyloid degeneration, it can be learned that it is the amount of fat in the cells embedded with the amyloid that determines the fat content of the latter. The cells walled off from the surrounding tissue by the amyloid became atrophic. They shrink

and disappear. When they contain fat it remains visible and can often be seen arranged about the remnants of a pyknotic nucleus. The endothelial cells of the liver with amyloid degeneration usually are filled with lipid droplets. Therefore the pericapillary amyloid shows much fat. The amyloid in the wall of the larger vessels contains little or no fat, because it has no direct relation to the fat-carrying cells.

The cholesterol fat diet does not increase the lipid content of the amyloid.

MEAT DIET

The effect of high protein diets has repeatedly been studied, especially from the standpoint of producing renal vascular lesions (Newburgh, Newburgh and Clarkson,²² Newburgh and Marsh,²³ Polvogt, McCollum and Simmonds,²⁴ Miller²⁵). Most of the experiments were made on rabbits and rats. Rats seem not to be affected by protein feeding (Miller). Mice also stand the high protein diet very well. They gain in weight and do not seem to be sick at any time, although the non-protein nitrogen content of their blood is distinctly higher than normal (table 1). The examination of the internal organs shows an enlargement of the spleen, liver and kidneys. No histologic changes are found in the kidneys nor in any other organ. With regard to Kuczynski's and Smetana's experiments with cheese feeding, it was of special interest that none of the control mice on beef heart powder diet developed amyloidosis, although this diet was given for more than 100 days.

Meat Diet and Nutrose Injections.—From Kuczynski's observations, it was to be expected that the meat diet would intensify or hasten the amyloid degeneration. But the meat diet did not only not favor the amyloidosis, it even protected the mice against it, and this to the same extent as did the cholesterol fat diet. Thus, one of the mice fed on meat showed no amyloid degeneration after as many injections as eighty-seven (table 3).

The chemical examination of the blood of the mice fed the high protein diet and receiving injections of nutrose, reveals that there is no constant parallelism between the increase of the nonprotein nitrogen in the blood and the appearance of amyloid in the organs. Thus, the nonprotein nitrogen of a mouse still free from amyloid after eighty-

22. Newburgh and Clarkson: Production of Arteriosclerosis by Diets Rich in Animal Proteins, *J. A. M. A.* **79**:1106 (Sept. 30) 1922; *Arch. Int. Med.* **24**:351, 1919.

23. Newburgh, Marsh, Clarkson and Curtis: Dietetic Factor in Etiology of Chronic Nephritis, *J. A. M. A.* **85**:1703 (Nov. 28) 1925. Newburgh and Marsh: Renal Injuries by Amino-Acids, *Arch. Int. Med.* **36**:682 (Nov.) 1925.

24. Polvogt, McCollum and Simmonds: *Bull. Johns Hopkins Hosp.* **34**:168, 1923.

25. Miller: *J. Exper. Med.* **42**:877, 1925.

seven injections was 76.9 mg., while it was 60 mg. in a mouse with beginning amyloidosis after sixty injections. The most marked increase of 184 mg. per hundred cubic centimeters of blood was found in a mouse with general amyloidosis after eighty injections.

COMMENT

The experiments reported prove the possibility of protecting mice for a considerable length of time against the harmful effect of repeated injections of foreign proteins which otherwise lead to amyloidosis in from five to eight weeks.

The mice are rendered more resistant by feeding large amounts of cholesterol and fat. They are protected as long as they are able to store the fat. The injections, however, finally cause the mice to lose this ability. The fat diet is then no longer effective, and amyloid appears in the different organs. It takes about twice as many injections to produce amyloid in a cholesterol fed mouse as it takes for mice on plain diet.

TABLE 4.—*Protein Diet*

| Days on Diet | Number of In- jections | Amyloid in | | | | |
|--------------------|------------------------------|------------|-------|--------|------------|-----------|
| | | Spleen | Liver | Kidney | Suprarenal | Intestine |
| 52 | 50 | 0 | 0 | 0 | 0 | 0 |
| 70 | 57 | 0 | 0 | 0 | 0 | 0 |
| 83 | 74 | + | 0 | 0 | 0 | 0 |
| 98 | 80 | +++ | ++ | + | + | + |
| 106 | 87 | 0 | 0 | 0 | 0 | 0 |

The most striking and the most significant changes are found in the liver whose cells take normally a part in the storage of cholesterol and neutral fat when large quantities of these substances are given with the food. After about the seventieth injection, the stored lipins gradually disappear from the liver cells. When amyloidosis starts later, there remains but little cholesterol and fat in the liver cells, or the cells are free from double refracting material. The fat which still can be found does not exceed the amount observed in the mice on plain diet with beginning amyloidosis.

Since the storage of excessive cholesterol and fat of the food is a normal function of the liver of the mouse, the disappearance from the liver cells of these substances preceding the onset of the amyloidosis suggests an impairment of the functional activity of this organ, associated with the metabolic disturbances causing amyloid degeneration. The disturbed liver function also explains the marked hypercholesterinemia of the mice with amyloidosis during digestion.

The cholesterol metabolism in cases of human amyloidosis has not been investigated, as, in general, metabolic studies in amyloid degeneration during life still are lacking. I think that such studies may help

more to a solution of this intricate problem than the chemical analysis of the amyloid substance itself and the most careful examination of its morphology.

Some observations in human amyloidosis can best be explained on the basis of a disturbed cholesterol metabolism. The liver does not yield peculiar microscopic findings. When amyloid is formed in the liver, it often is associated with isotropic fatty changes. Large amounts of cholesterol, however, are found in the kidneys showing advanced amyloid degeneration (Danish,²⁶ Fahr,²⁷ Munk²⁸). The anisotropic fatty infiltration of the amyloid kidney is excelled only by the lipid nephrosis (Fahr). Munk even emphasizes the close relationship between lipid nephrosis and amyloid degeneration. Windaus made his fundamental chemical analysis of cholesterol esters on amyloid kidneys.

What may bring about the accumulation of cholesterol compounds in amyloid degenerated kidneys has not yet been determined (Danish). Our observations offer the explanation that it is a disturbed liver function that causes an alteration of the cholesterol metabolism with an accumulation of the cholesterol in the blood (Danish). That the cholesterol is deposited in the kidney may partly be due to local circulatory disturbances resulting from the amyloid degeneration of the blood vessels. Circulatory disturbances favor the local precipitation of cholesterol (Lubarsch). Furthermore, an excretion of the cholesterol through the kidneys can be assumed on the basis of the studies of Gardner and Gainsborough.²⁹ Also in the mice with advanced renal amyloidosis, double refracting lipins were found in the epithelial cells of the convoluted tubuli.

No satisfactory explanation for the protection of the mice by feeding cholesterol can yet be given. The addition of cholesterol to the food is important, because the plain fat diet hardly increases the resistance of the mouse. Whether it is the storage of the cholesterol compounds in the liver that is essential, I do not know; but the drop of the body weight and the increase of the nonprotein nitrogen of the blood is delayed as long as the liver cells are filled with the lipins.

Feeding beef heart powder gives results similar to the cholesterol diet. According to Newburgh, beef heart powder contains about 81 per cent of protein. Cannon,³⁰ discussing the facts affecting the protein equilibrium, recently made the statement that "there has developed a considerable body of evidence that with abundant protein feeding the hepatic cells can store protein just as they can store glycogen" (and fat—author's remark). The stored protein apparently displays a pro-

26. Danish: *Verhandl. d. deutsch. path. Gesellsch.* **20**:307, 1925.

27. Fahr: *Handbuch der path. Anat. u. Histol.* **6**, G. Springer.

28. Munk: *Pathologie und Klinik der Nephrosen*, Urban and Schwarzenberg.

29. Gardner and Gainsborough: *Biochem. J.* **19**:667, 1925.

30. Cannon: *Am. J. M. Sc.* **171**:1, 1926.

tecting action, as do the cholesterol compounds. Or are the lipins of the beef heart muscle the important part? The total ether extract, lipins of all kinds, of the heart is between 2.86 and 3.73 per cent. Most of the lipin is phospho-lipin (Mathews³¹). Cholesterol is about 0.2 per cent of the dried muscle substance, and phosphatids are 8 per cent of the dried heart (Rubner³²). These quantities are too small to be of any significance.

The question will arise as to what may be the cause of the differences between the results of the experiments with beef heart and those with cheese. Feeding cheese, as reported by Kuczynski and Smetana, produces amyloid; beef heart powder may prevent it.

The meat powder apparently is a more suitable form of food rich in protein than is cheese. When Swiss cheese and bread are given, the mice often refuse the cheese after several days and rather starve than take it (Heiberg³³). They frequently suffer from intestinal disturbances and have more or less liquid stools. The intestinal mucosa is found to be edematous, with swollen and desquamated epithelium. It seems to me that the chronic enteritis resulting from the cheese diet, and not the flooding of the body with the split products of an abnormal protein metabolism, causes the amyloid degeneration. The mice that receive the beef heart do not show signs of intestinal irritation. They remain, therefore, free from amyloid.

CONCLUSIONS

Feeding (*a*) cholesterol and fat, or (*b*) dried beef heart powder increases the resistance of mice against the toxic action of long continued injections of foreign proteins. Thus, the formation of amyloid can be delayed for a considerable length of time.

The fat diet, however, is effective only when started together with the injections. If there is an interval between them, the beginning of the injections preceding the diet for more than two weeks, no protection of the mice can be noted.

The experiments with cholesterol reveal an alteration of the cellular activity of the liver immediately preceding the onset of the amyloid changes. The ability of the liver cells to store the cholesterol as double refracting spherocrystals is greatly reduced.

The difference between the effect of feeding cheese and beef heart powder is explained on the basis that cheese causes a chronic irritation of the intestine and thus may lead to amyloidosis, while the beef heart is a more suitable form of protein diet, does not affect the intestinal mucosa, and may even prevent amyloid degeneration.

31. Mathews: *Physiological Chemistry*, ed. 3, New York, William Wood & Company.

32. Rubner: *Klin. Wchnschr.* **4**:1849, 1925.

33. Heiberg: *Centralbl. f. allgem. Pathol. u. path. Anat.* **36**:433, 1925.

PRIMARY CARCINOMA OF THE FALLOPIAN TUBES *

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The occurrence of primary carcinoma of the fallopian tubes was first definitely established by Orthmann¹⁸⁰ in the case demonstrated in 1886 and fully reported in 1888.¹⁸¹ Previous to that time, its existence was disputed by such men as Birch-Hirschfeld and Bandel, and even as late as 1889, Schroeder unequivocally denied its occurrence. That these doubts were justified is shown by the fact that Orthmann¹⁸¹ was able to collect only thirteen cases from the literature of that period, all of them purely macroscopic descriptions, and the seat of the primary lesion being questionable. Doran⁴⁶ has unearthed an atlas of pathologic drawings containing a sketch by Renaud, dated 1847, of what apparently was a primary carcinoma of the tube. However, cancer of the ovary involving a hydrosalpinx might conceivably produce the same picture.

Since Orthmann's pioneer demonstration, numerous cases have been reported, and an extensive literature has arisen. In 1910 Doran⁴⁶ collected 100 cases, and in 1914 Vest¹⁹² added thirty-two more. Their tables, however, are not only incomplete, but several cases are listed more than once. For the sake of future workers, it may be well to point out these errors. In Doran's series, no. 14 Knauer and no. 33 Savor, no. 34 Arendes and no. 93 Von Franqué, no. 66 Orthmann and no. 78 Orthmann-Everke are the same cases; while in Vest's tables, Fonyó's cases and the first two reported by Wiesinger are not only identical, but are already listed by Doran under Dirner and Fonyó.

Inclusive of these 125 cases and the four here reported, I have been able to gather 196 cases. This number probably does not give a true picture of the frequency of the condition, as many escape diagnosis altogether, others are not reported, many are incomplete and not a few are doubtful.

A better idea of its comparative rarity can be formed from the following statistics: At the Leipzig Clinic (Zangemeister²⁰⁵), it was found in 0.31 per cent of all gynecologic laparotomies and in 1.33 per cent of those for diseased tubes. According to A. Martin,¹¹⁷ it occurred in 0.024 per cent of gynecologic laparotomies and in 0.34 per cent of those for tubal disease. In 19,000 gynecologic admissions to Kelly's service at Johns Hopkins Hospital, there were only four cases of primary carcinoma of the tubes (Vest¹⁹²), while at the Lenox Hill Hospital it was found four times in 5,870 specimens.

* From the Achelis Laboratory of the Lenox Hill Hospital.

ETIOLOGIC FACTORS

Age.—Primary carcinoma of the tubes affects women in the late preclimacteric and early postclimacteric period, 66 per cent being between the age of 40 and 55. The youngest victim was 27 (Norris), and the oldest 73 (Mantel) years of age. In table 1 the ages in 177 cases are arranged in half decades.

Sterility.—Reliable information as to the number of pregnancies is given in 147 cases in the series. One patient was a virgin. Disregarding abortions and miscarriages, sterility was present in forty-seven, or 32 per cent, and forty-three, or 29 per cent, bore but one child. If, with Vest,¹⁰² we consider the latter as cases of the so-called one child sterility, 61 per cent of the patients may be regarded as probably having had a pelvic infection. In addition, a number of the multipara had from one to many abortions. Another point that has been stressed is the fact that in the great majority of cases in which the data are supplied, the last pregnancy occurred many years before the onset of the illness.

TABLE 1.—Incidence of Carcinoma of the Tubes According to Age of Patients

| Age | Number | Percentage |
|---------------|--------|------------|
| 25 to 30..... | 3 | .. |
| 30 to 35..... | 6 | .. |
| 35 to 40..... | 23 | 13 |
| 40 to 45..... | 41 | 23 |
| 45 to 50..... | 44 | 25 |
| 50 to 55..... | 32 | 18 |
| 55 to 60..... | 22 | 13 |
| 60 to 65..... | 4 | .. |
| 65 to 70..... | 1 | .. |
| 70 to 75..... | 1 | .. |

However, it cannot be gainsaid that there are many cases, such as that reported by Novy, in which the child-bearing history is normal. The comparative frequency of sterility in these women has been advanced as evidence of the inflammatory etiology of this tumor.

Pelvic Inflammation.—In only 8 per cent of the cases is there any mention of a previous pelvic inflammation. Judging from the findings at operation, a much higher percentage is to be expected and probably could be elicited by careful histories. The adnexal inflammation in most cases followed an abortion. Several were subsequent to full term labors and one to a curettage. Only in isolated cases did the patient admit having had gonorrhea.

SYMPTOMATOLOGY

The symptoms are so varied and variable that it is difficult to construct a typical history. The most common complaints are pains in the lower part of the abdomen associated with a watery, often sero-sanguineous discharge and irregularities in the menses.

Pain.—This is practically a constant symptom, and differs from carcinoma of the fundus uteri in appearing early in the course of the disease. It is usually situated in the hypogastric, iliac or lumbar regions and on the same side of the lesion. It radiates frequently to the sacrum and lower extremities and occasionally to the rectum, when it is accompanied by tenesmus, or to the epigastrium. The character of the pain is variously described—pulling, pressing, sticking, boring, lancinating, cramplike. The last is the most common and most characteristic type and is often paroxysmal in character, its cessation coinciding with a sudden profuse discharge from the vagina. It may be more or less continuous, intermittent, periodic or associated only with the menses. Occasionally it is accompanied by fever, chilly sensations, nausea, vomiting or dysuria, and may, as in Warneck's and Stübler's cases, simulate an ovarian cyst with a twisted pedicle.

Discharge.—A discharge is present in the vast majority of cases. Its character, however, varies considerably. The most constant type is a profuse, watery, yellowish, serous discharge. Due to the frequent admixture of blood in various amounts and stages of decomposition, the fluid assumes a number of different hues, such as amber, tea, meat-water, brownish, rose or definitely bloody. Next in order of frequency is a white, purulent or leukorrheal discharge. In Novy's case it was described as being mucoid and in Spencer's 4, it had a greenish color. Often, a previously clear, watery discharge later becomes serosanguineous and a leukorrheal discharge becomes serous. At times a foul, offensive odor is noticeable. The discharge had a uriniferous odor in Goodrich's case. It is usually profuse, so much so that several patients (Boursier and Venot, Gemmel, Meyer) complained of being constantly wet. In fact, in Meyer's case the fluid was at first thought to be urine. In Danel 2, the discharge amounted to one liter a day. A characteristic syndrome, the so-called "hydrops tubae profluens" occurred in 10 per cent of the cases. In these cases, the discharge is periodic and accompanied by paroxysmal, cramplike pains, the latter usually diminishing or ceasing with the escape of the fluid. A coincident diminution in the size of the abdomen or of a palpable tumor is occasionally noticed (Routier, Mikhnov, Fabricius 2, Keitler). The duration of the discharge ranges from a few weeks to Saretsky's case in which it existed for twenty years. When the discharge has been present for a long time, it is leukorrheal, or was so at its inception.

Menses.—Menstrual abnormalities are common. Besides the usual changes incident to the menopause, the most common complaint is metrorrhagia. This often sets in after the climacterium has been established, and may be severe. Occasionally it is the only symptom (Bland-Sutton, Tweedy, Baisch-Raabe, Maiss, Kaarsberg and Barris). The

periods frequently become irregular, prolonged and profuse. Menorrhagia, dysmenorrhea and irregular intervals of amenorrhea are not uncommon, and may occur in various combinations. At times, the menstrual blood has a foul odor.

Enlargement of the abdomen is mentioned in about 15 per cent of the cases. The swelling is usually progressive and at times rapid. Its duration varies considerably, in one case (Knauer-Savor) commencing eighteen years before operation. The abdomen may undergo periodic diminutions in size associated with the discharge of a large amount of fluid from the vagina. Nine patients (Mikhnov, Fabozzi, Peham 1, Fonyó 1, and 2, Kundrat 1, Spencer 2, Vest 1 and Lewitzky) noticed or felt a tumor in the abdomen.

Urinary difficulties such as dysuria, urgency, frequency, incontinence, burning on micturition and retention occurred in 10 per cent of the cases in the series. They may be the only symptoms, and in two cases (Zangemeister 3 and Ruge 1), the sudden onset of urinary retention was the first indication of trouble.

Constipation and even obstipation are common symptoms. Tenesmus occasionally occurs, and in a case reported by Schottlaender and Kermauner mucus and blood were passed. Occasionally the patient complains of painful defecation.

In 20 per cent there was a history of loss in weight. It is qualified as rapid or marked in only a few cases.

Among the unusual symptoms are weakness, fatigability, feeling of heaviness in the lower extremities, swelling of the legs or ankles, headache, dizziness and fever. In Hare's case, the only complaint was sterility.

PHYSICAL OBSERVATIONS

There is nothing characteristic about the physical observations to differentiate the condition from an ovarian tumor or a chronic inflammatory affection of the tube. In addition, the picture is often complicated by the presence of concomitant pathologic conditions of the ovaries, the uterus, or both.

A mass is generally felt on one or both sides of the uterus, or, as is so common in diseased tubes, in the pouch of Douglas. Rarely it is felt in front of the uterus. The size of the tumor depends to a large extent on the presence or absence of an ovarian cyst, and varies in size from that of an egg to that of a man's head. It may fill the entire abdomen to the ensiform. Usually, it is described as being tensely cystic, fixed, or only slightly movable, and sausage or ovoid in shape. In about 10 per cent of the cases, however, it was hard, irregular and nodular. Small nodules are occasionally palpated in Douglas' pouch (Danel 2, Vignard.

Vest 2, Hillebrand). The tumor in several instances has grown larger during the period of observation (Fabricius 1, Kehrer, Salin).

Ascites was present in 10 per cent of the cases. This includes those in which it was recognized only at operation. On the other hand, it may be pronounced, as in the second case of Danel, in which 9 liters of amber-colored fluid were removed at one tapping.

Rarely the inguinal (von Rosthorn, Anufrief) or the supraclavicular glands (Danel, 2) are found to be enlarged. In Orthmann's third case, the inguinal glands became enlarged three months after operation, and in the cases of Rossinsky and the first case of Pfannenstiel, the supraclavicular glands became palpable three months and one year after operation, respectively.

Marked cachexia is rare. Anemia and undernourishment, however, are not uncommon observations.

DIAGNOSIS

From the foregoing description of the symptoms and physical observations, it is evident that a preoperative diagnosis of primary carcinoma of the tubes is extremely difficult. It has usually been mistaken for carcinoma of the ovary, ovarian cyst, chronic inflammatory adnexal disease, fibroids and cancer of the uterus. Although the diagnosis was suggested as a possibility by several authors, it was made definitely only once in this series. Falk,⁸⁹ in the first case that he reported, made a diagnostic puncture and removed a piece of tissue composed of polymorphous, round and irregularly polyhedral cells undergoing fatty degeneration. With the assistance of this examination, he claims to have made the correct diagnosis. He further urges that a puncture be performed in all suspected cases in which the tumor is adherent in the cul-de-sac. Other writers, such as Zweifel,²⁰⁷ on the other hand, point out the dangers and limitations of this procedure, and advise an exploratory laparotomy.

Falk⁸¹ has listed the diagnostic features as follows: (1) a woman around the menopause; (2) appearance and growth of a tumor without known cause; (3) profuse, serous, later bloody, discharge; (4) irregularities of menstruation; (5) curettage of uterus with negative results; (6) diagnostic puncture.

THERAPY

Owing to the insidious onset of the disease, the duration of the symptoms prior to operation is difficult to determine. Again, many of the symptoms are caused by preexisting pathologic states of the adnexa or uterus. Due to these factors, the range is wide—from a few days to twenty years. Except for two cases (Essex-Wynter and Mantel), all came to operation. Frequently, extensive metastases were already present, and in several the tumor could be only partially extirpated.

Radical operations were few, the surgeons, in the main, being contented with the removal of the diseased adnexa with or without the uterus. The tube was often ruptured during removal, with the escape of fluid and pieces of tumor tissue into the abdominal cavity.

COURSE

Follow-up statistics are very meager. A sufficient number, however, have been reported to show the highly malignant nature of the tumor. The results are extremely poor. Only six cases are reported as having no recurrence three or more years after operation, Fonyó, thirteen years; Zweifel 2, eight years; Veit, seven years; Benthin, five years, and Schenck and Legg, three years.

MACROSCOPIC FINDINGS

Von Franqué's⁶⁸ prediction that in the great majority of cases the tumor would be found to be bilateral, has not been borne out. The early preponderance of right-sided lesions has also been steadily cut down. In 183 cases in which the seat of the tumor is given, 64 were situated in the right tube, 62 in the left, and 57 were bilateral.

The affected tube usually has the appearance of a sactosalpinx, being variously described as having the shape of a sausage, retort, club, pear, tobacco pipe, horn, coil of intestine or spindle. It is usually greatly dilated, especially the pars abdominalis, markedly adherent and often tortuous and kinked. Occasionally it is twisted on its pedicle (Warneck, Stroganoff). The size of the tumor varies from the thickness of a little finger to that of a man's head. The latter are cases arising in a tubo-ovarian cyst. The abdominal ostium is practically always closed, while the uterine remains open. In a few cases, the tumor projects from an open ostium into the abdominal cavity. The tumor occasionally breaks through the serosa. Nodules or even papillary excrescences may be visible on the surface. The wall is usually thickened. In those cases in which the tumor apparently has originated in a hydrosalpinx, the wall may be as thin as paper.

The tumor, almost without exception, is situated in the middle or outer third of the tube, or in both. The pars abdominalis is the commonest seat of the lesion. Two main types of growth are recognized: a nodular and a diffuse. The nodular type is by far the most common and is usually situated in the ampulla of the tube, frequently extending into the median portion, however. It forms a cauliflower, papillary, friable, medullary mass, filling the lumen of the tube. It is usually grayish white, speckled with yellowish and red areas of degeneration and hemorrhage. Necrosis is frequent and sometimes extensive. Pieces of tumor tissue are often found free in the lumen or even in the uterine

cavity (Thaler). In the diffuse type, practically the entire inner surface of the tube is strewn with small nodular or papillary tumors.

The tube usually contains a varying amount of serous fluid which is often sanguineous. Occasionally it is brownish or chocolate colored. In a few cases it was viscid and mucoid or gelatinous and jelly-like. The jelly-like mass was greenish in Küstner's case. Pus was present in only four cases (Orthmann 1, Gurd, César, and one of our cases). The lumen was filled with caseous material at times, and in Fischel's case, the contents resembled rice soup.

The tumor readily metastasizes, and, as in carcinoma of the uterus, metastasis takes place by means of two different channels: (1) to the lumbar and inguinal; (2) to the hypogastric and sacral glands. Frequently, the uterus and ovaries are involved by retrograde propagation. Transplantation metastases to the peritoneal lining of the abdominal cavity, even as high as the diaphragm, are common. Naturally, the pelvic peritoneum, especially that covering the ovaries, uterus, bladder and opposite tube, is the portion usually affected. The mechanism of their occurrence is twofold, through an open abdominal ostium and by the growth reaching the serosa. At times, the contiguous structures, especially the ovary and uterus, are involved by direct extension of the tumor. Vascular metastases to the liver are rare. Several cases of implantation recurrences in abdominal or vaginal scars have been reported. It was present in one of our own cases.

Orthmann¹⁸⁴ was the first to point out the frequency with which a primary carcinoma arises in a tubo-ovarian cyst. In our series, it occurred in 10 per cent of the cases. An interesting case is that of Boxer 2, in which a bilateral carcinoma was present in two tubo-ovarian cysts. In a case reported by Rossinsky, the tumor originated in a tuboparovarian cyst, while in Orthmann 1 and in one of our own cases, a tubo-ovarian abscess was present.

Another common associated condition is a hydrosalpinx of the opposite tube, having been found in about 10 per cent of the cases. In fact, in several (Fehling, von Franqué 2, Norris), the carcinoma itself apparently originated in a hydrosalpinx. Twice the opposite tube was converted into a pyosalpinx (Orthmann 1, Tate) and twice into a hematosalpinx (Falk 2 and Kundrat 1).

The ovaries are usually small, atrophic, covered by adhesions, and cystic. Either ovary, in about 8 per cent of the cases, is found to be converted into a large ovarian cyst. The cysts may be bilateral (Danel 2) or intraligamentous (Borgna, Graefe, Vest 1, Robinson). In the case reported by Mériel, the cyst had undergone suppuration, and in Schottaender's a bilateral cystic fibro-adenoma was present.

As is to be expected from the average age of the patients affected, the uterus is frequently myomatous. This was true in 15 per cent of this series. Among the uncommon lesions of the uterus are polypi and endometritis.

Tuberculosis of the tubes, contrary to expectation, is rare. Besides the one here reported, five other cases are listed in our tables (von Franqué 4, Lipschütz, Barret, L'Esperance and Stübler). A tuberculoma of the opposite tube was found in the case published by Montgomery. Numerous authors (Alterthum,³ Orthmann,¹³² and Voight¹⁹⁵) have described the atypical epithelial growths of the tubal mucosa that occur in tuberculosis. In fact, as early as 1897, Bruno Wolff²⁰⁴ described adenomatous growths in such tubes simulating carcinoma, and predicted that future observations would discover a connection between chronic tuberculosis and primary carcinoma of the tubes. Orthmann and Münster¹²⁷ claimed to have demonstrated in those cases simulating a salpingitis pseudo-follicularis, an active proliferation of the inverted portions of the epithelium, and Böhmman²¹ showed that these glandlike structures were found at such depths that they could not have reached them without active growth. In spite of these facts and the comparative frequency of tuberculosis of the fallopian tubes, its association with carcinoma continues to be a rarity.

HISTOLOGIC STRUCTURE

Sänger and Barth¹⁵⁹ were the first to unite the various isolated observations and give a clear-cut description of the histologic structure of the tumor. They declared that every new growth arising from the tubal mucosa, including carcinoma, is papillary in character at its inception. Pseudo-alveolar formations are then produced by the union of the greatly branched papillae, although true alveolar collections of cells in the wall of the tube occur. They, thereupon, divided primary carcinomas of the fallopian tube into two groups: (1) purely papillary, (2) papillary-alveolar. This classification has been accepted by most gynecologists writing on the subject. Several modifications, however, have been advocated.

Friedenheim⁷² in 1889 reported a case of primary carcinoma purely alveolar in character, and suggested that it may have had its origin in an accessory tube or from an epithelial rest. On the basis of this observation, he added a third group to Sänger and Barth's classification—mural or pure alveolar carcinoma. Doran⁴⁷ rejects the accessory tube as the possible origin on the ground that its character in such a case would be an exact replica of that arising from the main tube. He believes that the remnant of the wolffian duct is a more likely origin. Several authors, such as Stolz,¹⁷⁸ doubt the necessity of considering the

case unique. They point out that the lumen of the tube was filled with detritus and the mucous membrane of the ampulla entirely destroyed, and that it may well have been a papillary-alveolar carcinoma which had undergone extensive necrosis or a metastasis from some unknown primary focus. A few other cases, such as those of Gosset and Eglington, are also described as being purely alveolar in character. They are, however, in all probability sarcomas.

Falk⁶¹ classifies the tumors as follows: (1) benign papillomas, (2) true carcinomas (atypical cells in glandlike structures penetrating the mucosa), (3) papillary epitheliomas (enormous overgrowth of the mucosa into papillae, spreading superficially at first).

Quénu and Longuet¹⁴⁵ advance the following classification: (1) typical cylindrical carcinomas, (2) metatypical or atypical carcinomas.

PATHOLOGIC TYPES

Papillary.—The normal tubal epithelium begins to proliferate and grow along the surface forming larger and larger papillary projections into the lumen. The papillae finally become greatly branched, the branches getting thinner with each division. The epithelium covering the papillae is single-layered, but may appear multiple due to the irregularity in the situation of the nuclei. The cells lose their cilia, become cubical or short-cylindrical, and their nuclei get larger and rich in chromatin. At the base, due to growth pressure, various papillae unite or appear to unite, forming intercommunicating cystlike spaces lined with cylindrical epithelium. Secondary foci in the tubal wall are produced by the closing-over of deep folds in the mucous membrane. The same type of growth takes place in the epithelial lining of these cysts—epithelial proliferation, branched papillary formations and finally solid alveoli. From the secondary foci, still deeper pseudo-alveoli can be formed. The final structure is therefore composed of three zones, which Sängner and Barth have named the inner maze, the middle straight zone and the outer pseudo-alveolar zone.

Papillary-Alveolar.—Due to the extremely rapid growth, the epithelial cells begin to grow into the tubal wall, forming true alveolar nests. The epithelial covering of the papillae becomes multiple and the cells more irregular and polyhedral. An increased number of mitotic figures is seen. At length, the tumor becomes completely atypical, infiltrating the musculature and metastasizing along the lymph channels.

The growth readily undergoes necrosis and frequently shows hemorrhages into its substance. Rarely, giant cells and cartilage are found. Epidermoidization occasionally takes place (Orthmann 3, Spencer 4, L'Esperance, Hillebrand).

Mixed tumors occur rather frequently but have not been included in the tables. In several cases (Falk, Zangemeister), after extirpation of an apparently pure carcinoma, the recurrence proved to be sarcoma. Again, in a few cases (Zweifel, Gosset, Eglington, Spencer 4, Penkert) it has been found difficult to determine whether the tumor should be classified as a carcinoma or a sarcoma.

In the case reported by Hofbauer, there was in addition to the tubal cancer, a squamous cell carcinoma of the cervix. Whether this is an autochthonous origin of two different malignant tumors in the genital tract or a metastasis to the uterus from a primary carcinoma of the tube, is difficult to decide. Von Franqué⁶⁸ and Quénu and Longuet¹⁴⁵ are inclined to the latter view.

The rôle that inflammation plays in the origin of the tumors is in dispute. Sānger and Barth¹⁵⁹ first expressed the opinion that primary carcinoma of the tube always occurs on the basis of a chronic inflammation of long standing, in all probability purulent at its commencement. In this view, he is supported by Orthmann.¹³⁴ Most of the other writers on the subject, such as Eckhardt,⁵¹ Zangemeister,²⁰⁵ Peham,¹³⁸ Stolz¹⁷⁸ and Quénu and Longuet¹⁴⁵ take issue with them.

Besides a more or less marked round cell infiltration about the tumor which was present in the vast majority of cases, direct microscopic evidence of inflammation of the affected tubes is given in only twelve cases (Merzelis, Hofbauer, Anufrief, Orthmann 3 and 4, von Franqué 2, Aichel, Norris, von Bubnoff, Einsle, César, Ruge 1). This is exclusive of those accompanied by tuberculosis. Of greater weight is the origin of the tumor in a tubo-ovarian cyst and the evidence of chronic inflammation in the opposite tube, both of which so frequently occur.

The closure of the abdominal ostium has been advanced as evidence of the inflammatory etiology of the tumor. The antagonists of Sānger and Barth, however, question its inflammatory significance and claim that the sealing of the ostium can be produced by the growth of a tumor in its vicinity.

The four cases here reported were all associated with inflammatory conditions; in the first there was a hydrosalpinx of the opposite tube; the second showed direct evidence of an old inflammation; the third was associated with chronic tuberculosis, and the fourth arose in a tubo-ovarian abscess.

Doran⁴⁷ contends that the carcinoma arises from a benign papilloma of the tube with or without the presence of inflammation. He is supported by Fearne⁶² and Kundrat,¹⁰¹ who point to such cases as that of Kaltenbach and Eberth, in which it was extremely difficult to differentiate the two. G. Müller,¹²⁵ however, considers the papilloma to be the

intercurrent stage between a chronic productive endomyo-salpingitis and primary carcinoma of the tube.

A number of demonstrations have not been tabulated because of the insufficient data furnished. These include three cases demonstrated by Amann⁶ in 1912 and a bilateral carcinoma reported by Hofmeier⁸⁵ in 1906. The one demonstrated by Amann⁶ in 1911 is apparently identical with that fully described by von Bubnoff.²⁰ Theilhaber and Edelberg¹⁸⁵ mention that they have seen four cases of primary tubal carcinoma. Spencer,¹⁵ in discussing Barris' case, states that he has seen a fifth patient with a carcinoma arising from a papilloma in a hydrosalpinx.

Several cases have not been included in the series because of their doubtful character. Kroemer⁹⁹ has reported briefly four cases of tubal carcinoma, one of which, however, was probably secondary to an intestinal carcinoma. The three primary tumors were all in association with tubo-ovarian cysts, but in only one of these was the origin definitely from the tube. This tumor microscopically proved to be a sarco-carcino-endothelioma. Violet's case¹⁹⁴ is in all probability a malignant myxoma. Ruge¹⁸⁷ refers to number 17 in Schottlaender and Kermauner's¹⁸⁸ series of cases with carcinoma of the uterus. They themselves regard the case as an adenocarcinoma of the uterus with an adenomyosalpingitis and a questionable incipient malignant adenoma of the tube.

Schmidlechner's¹⁸⁶ case has not been tabulated as the publication was not available.

The following cases of carcinoma, although doubtful, have been tabulated in this series because they have been published as such and are listed in various tables: Tate 2, Pfannenstiel 1 and 2, Hare, Gosset, Eglington, Penkert, Spencer 4, and Gurd.

CASE REPORTS

CASE 1.—History.—F. G., aged 39, German, a housewife, was admitted on Feb. 15, 1911, complaining of metrorrhagia. Her periods had been regular up to eighteen months before, when constant bleeding between periods had set in. There was no pain or leukorrhea. Her menses began at 15, were regular and profuse, lasting seven days. She never had been pregnant.

On pelvic examination, a tensely cystic mass, the size of a fist, was palpated in the right fornix.

Diagnosis.—Right tubo-ovarian disease.

Operation and Course.—Bilateral salpingo-oophorectomy was performed, Feb. 17, 1911. The patient made an uneventful recovery.

On Nov. 2, 1911, she was readmitted with a recurrence, the size of a tangerine, in the abdominal wall. This was resected on November 4. On April 11, 1912, she was again admitted with a similar recurrence at the site of the previous operation. This tumor and two omental nodules were excised, April 21, 1912.

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature

| No. | Author | Age | Children; Menses | Symptoms | Physical | Duration | Operation | Side | Macroscopic | Microscopic | Course |
|-----|-----------------------------------|-----|---|---|---|----------------------|---|----------------|--|---|--|
| 1. | Orthmann.... (136, 131) | 46 | Doubtful abortion | Pain and swelling of lower part of abdomen; moderate leukorrhea | Mass, size of child's head, right side, smaller one behind uterus | Seven to eight weeks | Removal of tube | Right | Right tubo-ovarian abscess; papillomatous growths in ampulla, with slight involvement of walls of uterus; small metastases to uterine vesical pouch and to small pelvic gland; suppurative mass growing from tubal walls; ostium closed; sanguinous serum in canal; metastases to right ovary; old inflammation of left adnexa | Papillary alveolar carcinoma | Died 6 days postoperative |
| 2. | Doran..... (43) | 43 | 1-22 years ago; menopause at 47½ | Watery, inoffensive, occasionally bloody discharge; perimetritis after curettage | Tumor on right side..... | Three years | Removal of tube | Right | Large, soft, cancerous mass growing from tubal walls; ostium closed; sanguinous serum in canal; metastases to right ovary; old inflammation of left adnexa | Papillary alveolar carcinoma | Recurrence, 10 months and 3 weeks postoperative |
| 3. | Kaltenbach and Eberth (90, 91) | 59 | Sterile; dysmenorrhea; menopause at 49½ | Serosanguineous discharge; pain in right half of pelvis and right sacro-iliac region, radiating to stomach and lower extremities | Mass, size of a fist, on right side, and size of plum on left; small subperitoneal myoma | Four years | Removal of tube | Right and left | Papillary outgrowths in both tubes infiltrating wall and reaching peritoneum on right side | Papillae and cystlike spaces filled with papillae lined with single layer of epithelium | Recurrence, 18 months postoperative |
| 4. | Velt..... (160, 191) | 36 | Sterile | Marked pains and low temperature | Mass on left side of pelvis | "For a long time" | | Left | Inner surface of tube covered with numerous small outgrowths; contents ragged and malodorous | Carcinoma | |
| 5. | Essex-Wynter (54) | 50 | Sterile? | Discharge of blood for a few months; hypogastric pains | | Four months | | Right | Mass, the size of bantam's egg, in connection with fimbriated end of tube | | |
| 6. | Landau and Rabinstein (100) | 46 | Sterile; regular | Pains in lower abdomen, 3 years ago; for 11 weeks severe pains on left side radiating to posterior surface of thigh | Mass, size of fist, on left side; smaller one on right | Two years | Removal of tube | Right | Left hydrosalpinx; right tube filled with a soft pulpy mass | Papillary alveolar carcinoma | Recurrence within 10 months |
| 7. | Zweifel..... (207) | 46 | One child; regular | Watery, yellowish discharge; pains in abdomen and weakness | Prominence of lower part of abdomen due to 2 tumors as large as head of a child; one on the right sausage-shaped; the other round | Nine months | Hysterectomy; double salpingo-oophorectomy | Right and left | Both tubes greatly enlarged, tortuous and filled with papillary growths; uterus and ovaries free | Papillary alveolar carcinoma | "Lived for about 1½ years" |
| 8. | Westermarck and Quensel (201) | 45 | One child, 20 years ago; regular up to 5 or 6 years ago; then severe dysmenorrhea | Severe metrorrhagia; pains in lower part of abdomen; constipation | Large, cystic swelling on both sides of uterus; larger on the right side | One year | Double salpingo-oophorectomy | Right and left | Right tube filled with cauliflower-like growth; left with small papillary excrescences; metastases to right ovary; at necropsy, liver, uterus and pelvic glands showed metastases | Carcinoma, most advanced in right tube | Recurrence, 2 months, and death 5 months postoperative |
| 9. | Routier..... (156) | 60 | Sterile; menopause at 50 | Enlargement of abdomen and progressive weakness, 2 years; 1 year ago and again at 6 months pains in left side of abdomen and discharge of a large amount of yellowish fluid with diminution in size of abdomen; at times swelling of left leg | Hard tumor, the size of a child's head, on left side | Two years | Hysterectomy; left salpingo-oophorectomy; right salpingectomy | Left | Tube dilated like coil of intestine; abdominal end forms a cyst, the size of a child's head, and contains papillomas; one-half liter of dark, blackish acetic fluid; no metastases | Papillary alveolar carcinoma | |
| 10. | Smyly..... (176) | .. | | | | | Rectum opened in two places | Unilateral | | Carcinoma | Died postoperative |

| | | | | | | | | | |
|--|---|---|---|-------------------------|---|----------------------|--|---|--|
| 11. Stroganoff... .. (160) | | Alternating amenorrhea and menorrhagia; severe pains in right lower part of ab- domen | Ovoid tumor on right side; large, fixed, retro- verted uterus | One year | Curet- tage; double sal- pingo-oophor- ectomy | Right | Tube twisted on its pedicle and its outer portion dilated to size of an egg which on section contained a friable, cauliflower, cherry-sized mass | Adenocarcinoma arising from the mucous membrane | Well at 1 year (Doran) |
| 12. Tuffier..... 55 (187) | Two, 33 and 30 years ago; regular; meno- pause at 51 | Pains in abdomen and metrorrhagia | Fluctuating tumor in re- gion of right adnexa filling pouch of Douglas and pushing uterus toward symphysis | Two months | Right sal- pingo-oophor- ectomy | Right | Tube formed a pear-shaped tumor the size of a child's head; walls hypertrophied; in a circumscribed area, 1 cm. in diameter, a blackish, crumbly papillary mass | Papillary car- cinoma; many accessory epi- thelial tubes | Recurrence 6 months, and death 1 year post- operative |
| 13. Cullingworth and Shattock 60 (35) | Sterile; menopause at 51-52 | Severe pain for 1 week in right iliac region 4 months ago; recurrence 1 month later, present since; en- largement of abdomen and presence of lump; obstipa- tion for 20 days; loss of weight | Ascites; hard nodular tu- mor in hypogastrium and two superficial nod- ules to right of this | Four months | Right sal- pingo-oophor- ectomy | Right | The right tube infiltrated by a new growth with extension into the broad ligament; large right ova- rian cyst; omental nodule implicat- ing bladder; metastases to wall of cyst | Infiltrating epi- thelioma; near ex- ternal surface, cystic spaces lined with cylindrical epithelium and papillary processes | Well 8 years later |
| 14. Zweifel..... 41 (308, 205) | Five children; regular | Curet- tage for menorrhagia 2 years ago; cramplike pains in lower part of abdomen, especially on right side | Round, tense, elastic tu- mor, size of man's head, on right side and in pouch of Douglas | One year | Hysterectomy; double sal- pingo-oophor- ectomy | Right | Outer portion of right tube con- verted into a thin sac containing thin brownish fluid and soft tumor masses; small amount of ascitic fluid | Carcinoma papillare | |
| 15. Warneck..... 43 (197) | Three, the last 12 years ago; regular; profuse | Sudden pain in lower abdo- men; fever and dysuria after exercise | | | Hysterectomy; double sal- pingo-oophor- ectomy | Right and left | Both tubes enlarged; right tubo- ovarian cyst in ampulla of which was a cauliflower mass; a more pedunculated tumor in left tube; ovaries and uterus free | Carcinoma papillare | Died 3 weeks later following an operation for intestinal obstruction |
| 16. Knauer-Savor 58 58 (95, 161) | One, 31 years ago; meno- pause at 46 | Abdomen began to enlarge 18 years ago to size of 7 months' pregnancy; then re- mained stationary; severe pains in lower abdomen and incontinence of urine on walking; loss of weight | Very large cystic tumor occupying almost the whole of abdomen | One year | Incomplete hysterec- tomy | Right | Very large right tubo-ovarian cyst; in dilated middle portion of the tube, a papillary medullary tumor the size of a pigeon's egg; myoma of fundus uteri | Papillary carcinoma | |
| 17. Fischel..... 40 (94) | One abortion; regular before present illness | Yellowish, profuse discharge for a long time; pains in lower part of abdomen, 7 months; after 3 months amenorrhea, return of menses with diminution of pain; loss of weight | Large, spherical tumor on right side and sausage- shaped one on left | Over seven months | Right sal- pingo-oophor- ectomy | Right | Right tube retort-shaped and filled with rice soup fluid; papillomatous nodules on serosa | Papillary alve- olar carcinoma; metastases to serosa | Died 7 months postoper- ative |
| 18. Mikhov..... 46 (121) | Three, the last 24 years ago; regular | Amenorrhea and metror- rhagia 8 years ago; fist- sized tumor in lower part of abdomen which always disappeared at end of month; colicky pains; serous discharge | Elastic, fixed tumors, 1½ times a fist in size, be- hind and to both sides of uterus | Eight months | Double salpingo- oophorec- tomy | Right and left | Left tube larger than a fist, sausage- shaped and filled with small, yel- lowish-gray growths and serous- guineous fluid; right tube also en- larged; its wall thickened, tortuous and ostium closed; in pars abdom- inalis, pea-shaped papillary growths and serohemorrhagic fluid | Multilayered pap- illary carcinoma infiltrating wall of tube; epi- thelium present | Recurrence 7 months postoper- ative |
| 19. Singer and Barth 45 (169) | One, 20 years ago; regular; scanty | Bloody and serosanguineous discharge practically daily; symptoms of pansalpin- gitis | Retverted uterus; irreg- ular tumor on right side which grew larger and tender; small inflamma- tory mass, left | Five months | | Right | Kidney-shaped tumor in outer two thirds of right tube, filled with a medullary tumor; no sign of fun- dus; left tube the seat of a pan- salpingitis and perisalpingo- oophoritis chronica | Papillary and pseudo- alveolar carcinoma | Well 7 months later |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menstruation | Symptoms | Physical | Duration | Operation | Side | Macroscopic | Microscopic | Course |
|-----|--------------------------|-----|---|--|--|------------------------|--|----------------|---|---------------------------------------|---|
| 20. | Ferne..... (62) | 56 | Married | Serosanguineous discharge; burrowing on urination | Irregular tumor, size of hen's egg, in region of right adnexa | One and one-half years | Right salpingo-oophorectomy | Right | Right tube sausage-shaped; in ampulla and infundibulum a compact, white, pulpy tumor; abdominal ostium closed; ovary free | Papillary alveolar carcinoma | Well 19 months postoperative |
| 21. | Von Rosthorn (155) | 59 | One, 20 years ago; menopause at 53 | Serous discharge showing marked changes in quantity and which recently became purulent and ex-coriating | Cystic tumor on right side; enlargement of inguinal glands | Three months | Vaginal hysterectomy; right salpingo-oophorectomy; resection of inguinal glands 6 months later | Right | Right tube sausage-shaped; ampulla dilated and filled with an encephaloid, crumbly, purulent mass; salpingitis interstitialis; right ovary free; uterus shows a residual perimetritis; at necropsy, metastases to retroperitoneal, iliac and inguinal glands with compression of inferior vena cava and thrombosis of left external iliac vein, to the vaginal wound and to the left tube | Papillary alveolar carcinoma | Died 6 months after first operation, following resection of inguinal glands |
| 22. | Osterloh..... (136, 137) | .. | .. | | | | Salpingectomy | | Tube resembling pyosalpinx adherent to abdominal wall | | Recurrence abdominal wall, 1 year post-operative |
| 23. | Miller..... (126, 134) | 49 | One, 34 years ago; irregular for 4½ years | Pain in lower part of abdomen; swelling of abdomen; loss of weight | Large cystic tumor extending above umbilicus on right side and an elastic resistance in pouch of Douglas | Seven months | Right salpingo-oophorectomy; left salpingectomy | Left | Left tube like a hydrosalpinx; horn-shaped, tortuous, the size of a goose egg and filled with serous fluid; the uterine end is changed to a stiff tube containing fine papillary growths; right intraligamentous cyst; right tube and left ovary normal | Papillary alveolar carcinoma | |
| 24. | D'Anna..... (41) | 44 | Married | Bloody vaginal discharge.... | Slightly tender cystic tumor, size of a citron, in lower right quadrant | | Right salpingo-oophorectomy | Right | Tube did not appear normal; right ovarian cyst | Carcinoma infiltrating wall | |
| 25. | Watkins-Ries (198, 147) | 45 | Married | Dysuria and pain in pelvis... | Masses to both sides of fibroid uterus | Ten days | Panhysterectomy | Right and left | Both tubes containing papillary tumors with metastases along the subserous lymphatics to the broad ligaments, ovaries and uterus; adenomyoma of right tube; fibroid uterus | Papillary carcinoma | Recurrence, 3 months post-operative |
| 26. | Pillet..... (145) | 55 | | | Tumor of right adnexa.. | | | Right | Tumor of right tube involving the cortical portion of right ovary | Papillary alveolar | |
| 27. | Eckhardt..... (51) | 45 | Sterile; irregular; dysmenorrhea | Backache; dysuria; difficulty in defecation; pains in lower part of abdomen radiating into left thigh; loss of weight; increase in size of lower part of abdomen; discharge for a short time at beginning of illness | Slightly nodular and elastic, tender mass in region of left adnexa, the size of a child's head | One month | | Left | Distal end of tube suddenly dilates into sac, the size of a child's head, and contains grayish-white, encephaloid, cauliflower growths; abdominal ostium closed; small metastases to mesosalpinx and broad ligament | Papillary alveolar carcinoma | Well a few months post-operative |
| 28. | Boldt..... (23) | .. | | | Rupture of tube during examination | | Vaginal salpingo-oophorectomy | | Looked like ectopic gestation..... | In all probability, primary carcinoma | |

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| 29. Falk..... 53 (59) Married | Sterile; regular; menopause at 47 | Pains in left lower extremity radiating into left leg for 3 months; bloody discharge for 3 days; chilly sensations for 8 days; prolapse of uterus for 2 years | Fixed, cystic tumor, as large as a fist, in region of left adnexa; on diagnostic puncture, removal of tissue composed of irregular polymorphous and round cells | Three months | Vaginal pan-hysterectomy, right ovary left behind | Left | Left tube dilated, abdominal ostium closed and contained a papillary adnexa normal; the left ovary and right adnexa normal; at necropsy, recurrence in vaginal wound with rupture into bladder and a large retro-peritoneal mass | Papillary alveolar carcinoma; recurrence showed sarcoma | Recurrence 5 months postoperative |
| 30. Falk..... 45 (60, 61) | One child; regular before illness | Irregular menses and continuous foul serous discharge which later became blood-tinged and finally dirty brown; recently pains in left side of abdomen; loss of weight | Cystic tumor, size of pregnancy, to the right and behind uterus; under observation, grew to size of a man's head, and tumor size of a hen's egg appeared on left side | Six months | Curettag; vaginal pan-hysterectomy | | Right tube larger than a child's head; ampulla sac-like and contained hemorrhagic fluid and grayish-white, papillary growths; left hematosalpinx; right ovary cystic; uterus and left ovary normal | Papillary carcinoma | |
| 31. Roberts..... 43 (148) Married | Sterile; periods more frequent in past year | Several attacks of severe pains in lower part of abdomen; persistent watery discharge; occasionally bloody; loss of weight | Tumor in region of right adnexa | Eleven months | Right salpingo-oophorectomy; left salpingectomy | Right | Right tube the size of a bologna sausage; abdominal ostium closed; filled with a papillomatous growth except for 1 cm. of uterine portion; left tube inflamed; right ovary small and cystic | Papillary alveolar carcinoma | Well 14 months post-operative |
| 32. Hofbauer..... 46 (84) Married | Three, the last 25 years ago; regular up to 3 years ago | White discharge; attacks of sticking pains in left lower abdomen; menorrhagia; rapid loss of weight | Uterus enlarged; tumor size of hen's egg on left side | One year | Curettag of cervix; pan-hysterectomy | Right and left | Right tube spindle-shaped; swelling toward abdominal end and filled with a cauliflower tumor; left tube S-shaped, ampulla dilated and retort-shaped and filled with a similar tumor; the abdominal ostium closed; uterine myoma; cervical polyp; small ulcer on its posterior wall | Curettings from cervix showed squamous cell carcinoma; tubes; papillary alveolar carcinoma; myositis; endosalpinx; endosalpinxitis pseudo-follicularis | |
| 33. Roberts..... 60 (149) Married | Sterile; menopause at 50 | Intermittent attacks of severe pain in lower part of abdomen; serosanguineous discharge | Mass in region of left adnexa and in pouch of Douglas | Ten months | Double salpingo-oophorectomy | Left | Pars externa of left tube much distended and sacculated, containing degenerated villous growth; left ovary enlarged and cystic; right adnexa normal | Papillary alveolar carcinoma | Recurrence 8 months postoperative |
| 34. Pfannenstiel..... .. (140, 141) | | | | | | | Papillary tumor, size of a walnut, at the junction of the tube in a tubo-ovarian cyst | Primary carcinoma | Death 1 year postoperative |
| 35. Pfannenstiel..... 53 (140, 141) | Sterile | Swelling of abdomen..... | Tumor extending almost to umbilicus | One year | | Right and left | Similar to above, except for a few small excrescences on inner wall of cyst | Primary carcinoma | Death 2 months following operation for cancer of stomach |
| 36. Daniel..... 45 (38) | One, 25 years ago; regular; profuse | Heaviness in lower extremities; fatigue; for some time, discharge and loss of weight | Nodular, fixed tumor smaller than a fist in posterior and left fornix | Eight months | Left salpingo-oophorectomy | Left | Left tube sausage-shaped, half a fist in size, with nodules and streaks on surface; filled with a grayish-red, soft, pedunculated growth and a little yellowish fluid; metastatic nodules in left horn of uterus | Papillary alveolar carcinoma | Recurrence in right tube and then in pelvis and abdominal wall |
| 37. Daniel-Duret..... 46 (38, 50) Married | Two, the last 4 years ago | Enlargement of abdomen, which was tapped twice | Tumor in left flank; small hard nodules between navel and symphysis and several the size of grapes in left fornix; enlarged supraclavicular glands | Four months | Double salpingo-oophorectomy; curettag; metastases in pelvis | Right and left | Ampullae of both tubes dilated, orange-sized tumor growing out of ostium; multilocular cysts of both ovaries with a few vegetations on surface; large pelvic metastases | Papillary multilayered carcinoma with atypical epithelium in places | Recurrence in a few weeks |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menses | Symptoms | Physical | Duration | Operation | Side | Macroscopic | Microscopic | Course |
|-----|---------------------------|--------------------|--|--|--|--------------------|---|-------------------|--|---|--|
| 38. | Jacobson.... (57) | 45 | One miscarriage 22 years ago; menopause at 44 | Metrorrhagia; severe pain; profuse serous discharge associated with cramplike pains in lower part of abdomen | Soft, fixed tumor, size of egg, in pouch of Douglas; no fluid on punc- ture | One year | Vaginal left sal- pingectomy; right salpingo- oophorectomy | Left | Soft, grayish-red masses projecting from torn portion of tube which contains a serous fluid | Papillary alveolar carcinoma | |
| 39. | Fabrielus.... (38) | 41 | Many; regular, more profuse at present | Watery discharge; pains in left side and sacrum radi- ating into left thigh; difficulty in defecation | Enlarged left tube as big as a plum at abdominal end; after operation right tube greatly enlarged and cavity filled with papillomatous masses appeared at site of operation | One year | Vaginal left sal- pingectomy; biopsy; curet- tage of cavity | Right | Enlarged left tube containing a plum-sized mass in its abdominal portion; bladder involved | Papilloma of left tube; curetings showed carcinoma | Condition very bad 6 months after last operation |
| 40. | Fabrielus.... (38) | 41 | Two children, two abortions | Severe pain in right side of pelvis, 18 months; for 6 months, watery, profuse discharge after periods associated with diminution in size of tumor and les- sening of pains | Tumor larger than a fist on the right side | Eighteen months | Vaginal right salpingo-oophor- ectomy; left adnexa and uterus removed 6 months later | Right | Right tubo-ovarian cyst; tube filled with soft, pulpy masses; ovary negative; at second operation, re- currence at site and metastases to uterus, peritoneum and intestines | Papillary alveolar carcinoma | Recurrence a few months after oper- ation |
| 41. | Friedenheim (72) | 35 Mar- ried | Three, the last 4 years ago; regular; profuse | Pains in abdomen, especially on left side and in sacrum; white discharge; rapid loss of weight | Hard, mobile tumor, larger than fist, on right side | Nine months | Right salpingo- oophorectomy | Right | Enlarged right tube adherent to large intestine; tumor in middle third involving sacra; metastases to left parametrium | Pure alveolar car- cinoma; mucous membrane and muscularis in pars abdominalis practically destroyed | Recurrence 3 months postoper- ative |
| 42. | Brennecke.... (26, 26) | 49 | One, 25 years ago; regular | Watery, yellowish discharge, several months; continual abdominal pain for 5 weeks | | Several months | | Right and left | Tubes converted into sacs like large intestines and markedly adherent; uterus not enlarged | | Recurrence 3 years later |
| 43. | Scharlieb.... (163) | 55 Married | Menopause at 50 | Hypogastric pains tempo- rarily relieved by yellow discharge streaked with blood; loss of weight; painful defecation | Round, elastic mass in left fornix | Four months | Left salpingo- oophorectomy | Left | Left tube flask-shaped in its outer third and spiral in its inner third; the former the size of a bantam's egg and containing a papilloma- tous growth | Malignant papilloma | Death, 25 months post- operative |
| 44. | Wittbauer.... (203) | 35 | One child; regular; meno- pause at 53 | Pulling pains in lower part of abdomen; loss of weight | Resistances in both for- nices | Four months | | Right and left | Right tube the size of a child's head and divided into three portions; the first, the size of an apple, con- tained brownish fluid; the second containing a pulpy mass the size of a walnut, and the third, larger than a fist, formed an hematomatous plug; the left tube divided into two portions, the medial one con- taining a walnut-sized growth | Papillary alveolar carcinoma | Well 3 months postoper- ative |
| 45. | Novy.... (129, 46) | 70 Widow | Ten children | Occasional slight serosan- guineous mucoid dis- charge; hypogastric pains | No tumor; curetings showed carcinoma | | | Right | Right tube retort-shaped and filled with caseous, carcinomatous masses; the abdominal ostium closed; polypoid hypertrophy of uterine mucosa; right ovary atrophic | Papillary car- cinoma; chronic oophoritis; metritis and endometritis interstitialis | Recurrence 2 years post- operative and death 5 months later |

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|------------------------------------|--|--|--|----------------|---|----------------|---|--|--|
| 43. Merrells..... 35 ? (116) | Questionable abortion 15 months ago; dysmenorrhea | Irregular; frequent profuse menses; headache; constant pain in left side of abdomen, back and both legs | Orange-sized, posteriorly on the right side and smaller tender mass on left | Fifteen months | | Right | Right tube retort-shaped and containing numerous papillomas increasing in size as they approached the para abdominalis and continuous with the ovary; abdominal ostium closed | Right tube: papillary alveolar carcinoma with involvement of ovary; chronic salpingitis of both tubes | Recurrence 20 months later |
| 47. Von Franqué- Ardes (12, 65) | Two children; regular; menopause at 51 | Metrorrhagia and moderate discharge; recently, pains in lower part of abdomen and sacrum; slight bleeding and swelling of left leg | Uterus enlarged and pushed to the right by an indefinite cystic mass of left adnexa extending to umbilicus | One year | Double salpingo-oophorectomy (right ovary not removed); vaginal hysterectomy 5 months later | Right and left | Right tube the size of two coals of intestine; the ampulla the size of an apple; the lumen almost completely filled with a homogeneous tumor cauliflower in structure in the para abdominalis; left tube containing a cauliflower; papillary mass 3 cm. from the uterine end which had broken through the wall and was growing free in the abdominal cavity; ostium closed; left large ovarian cyst with papillary growth on outer surface; metastatic nodules in left mesosalpinx; small adenocarcinoma in left cornua of uterus | Papillary alveolar carcinoma | Metastases to uterus 4 months post-operative; death from recurrence 1½ years later |
| 48. Von Franqué 52 (66, 70) | Menopause at 46 | Boring pains on right side.. | Tense elastic club-shaped tumor on right side showing irregularities on its surface and extending almost to navel; dense diffuse infiltration toward pelvic wall and mass twice the size of a bean on anterior pelvic wall | Three weeks | Panhysterectomy; incomplete removal | Right | Right tube and ovary changed into large carcinomatous tumors; metastatic nodules on surface of left tube, uterus, bladder, peritoneum, and both ovaries | Papillary alveolar carcinoma; chronic salpingitis pseudo-follicularis; entire lymphatic system of uterine mucosa full of carcinoma | |
| 49. Hurdon..... 53 (86) | Four children | Almost constant blood-tinged discharge; frequent fever | Mass on left side..... | One year | Left salpingo-oophorectomy | Left | Dilatation of abdominal end in a cylindrical mass filled with granular, friable, papillary growths; fibrated end replaced by the decapsulated mass from which a papillary excrescence projected into a cyst of the ovary | Papillary alveolar carcinoma | Recurrence 2 years post-operative |
| 50. Hanneart.... 57 (80) | Nine children; one miscarriage; menopause at 55 | Lancinating pains in lower part of abdomen radiating to sacrum and thigh; purulent, later bloody discharge; loss of weight | Hard, nodular tumor the size of a child's head, on left side | One year | Left salpingectomy | Left | Cystic tumor the size of a fetal head formed by the left tube; abdominal ostium closed; lumen filled with cauliflower vegetations, debris and pinkish mucous fluid blood-tinged in places | Papillary carcinoma | |
| 51. Boursier and Venot (24) | Four, the last 30 years ago; regular; menopause at 43 | Lancinating pains in right iliac region; profuse watery, occasionally bloody discharge; loss of weight | | Three years | Right salpingo-oophorectomy | Right | Right tube formed a pear-shaped, soft tumor the size of two fists, filled with numerous soft, reddish-white vegetations | Papillary carcinoma | Well 10 months post-operative |
| 52. LeCount..... 47 (106) | One, 21 years ago; many miscarriages; dysmenorrhea for 2 years | Increasing prolapse of uterus; swelling of abdomen; constant leukorrhea sometimes streaked with blood | | Two years | Left salpingectomy; colporrhaphy; exploratory 9 weeks later | Left | Marked ascites; abdominal end of the left tube dilated, fibria gone and was seat of an exuberant, cauliflower growth which had broken through the wall; lumen filled with soft necrotic tissue | Papillary alveolar carcinoma | Extensive recurrence 9 weeks post-operative |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menes | Symptoms | Physical | Dura- tion | Operation | Side | Macroscopic | Microscopic | Course |
|-----|-----------------------------|-----|---|---|---|---------------|------------------------------|----------------|---|-----------------------------------|---|
| 53. | Quénou and Longuet (145) | 42 | Regular | Profuse discharge; curettage and polyp removed, but discharge persisted; metrorrhagia | Tumor extending to umbilicus | | Panhysterectomy | Left | The left tube more than two fists in size, soft, fluctuating and blackish in places, containing a brainlike tumor; right hydrosalpinx; fibroid uterus; right ovary normal; left not found | Papillary alveolar carcinoma | Well 2 years postoperative |
| 54. | Quénou and Longuet (145) | 51 | One, 31 years ago; regular; menopause at 50 | Pains in back and abdomen, especially on left side; constipation; profuse leukorrhea for 1 month; recently a severe metrorrhagia | Tumor in right fornix and one on anterior surface of uterus | Three months | Panhysterectomy | Right | Right tube contained a bean-sized, smooth, hard, grayish-black tumor 3 cm. from the ampullary end; abdominal ostium closed; right ovary cystic; very large fibroma of uterus | Preponderately alveolar carcinoma | Died 2 years and 1 month postoperative |
| 55. | Peiham and Knauer (138, 90) | 47 | Four children, one miscarriage; regular; dysmenorrhea | Swelling of abdomen for 6 months; tumor in left lower abdomen present for 2 months; has grown very rapidly in past 5 weeks; moderate pain in abdomen and sacrum; lump in right breast | Large cystic tumor in median line extending a hand's breadth above symphysis and on left side to costal arch; tubular structure to right of uterus; small, somewhat nodular, tender tumor mass size of a pigeon's egg in posterior fornix | Six months | | Right and left | Left tube size of a child's head, abdominal portion being dilated into a retort-shaped sac; no sign of fibrosis; at junction of middle and outer thirds, papillary tumor; right tube enlarged and thickened, containing two grayish-red papillary tumor masses, size of a hazelnut and walnut, respectively; abdominal ostium open; left ovary cystic, showing metastases; right ovary converted into a cyst the size of a child's head, also showing metastases; metastases to pelvic peritoneum | Papillary alveolar carcinoma | Recurrence 6 months postoperative in posterior wall of vagina; excised; death 13 months later; necropsy |
| 56. | Gracia (77) | 51 | Sterile; regular to 9 months ago; then premature and profuse | Hemorrhages; pelvic pain; hypogastric swelling | | | | Left | Left tube the shape of a tobacco pipe, as large as a fist, filled with serous fluid and containing a papillary tumor in its ampulla; right intraligamentous mass, size of a large potato springing from the mucosa of the middle and outer portions of right tube; pedunculated cancerous nodule of endometrium 1 cm. below orifice of right tube; left tube normal | Papillary alveolar carcinoma | Well 8 months postoperative |
| 57. | Fabozzi (56) | 48 | | | | Seven months | Panhysterectomy | Right | Deeply lobulated mass, size of a large potato springing from the mucosa of the middle and outer portions of right tube; pedunculated cancerous nodule of endometrium 1 cm. below orifice of right tube; left tube normal | Papillary alveolar carcinoma | Died 4 days postoperative with peritonitis |
| 58. | Ponyó and Diner (58, 67) | 50 | Two children, one abortion; menorrhagia; dysmenorrhea; postmenstrual serosanguineous discharge; menopause at 48 | Tumor in "stomach" which increased in size in past 4 months | Hard, nodular tumor extending above symphysis on right side and one in anterior left fornix continuous with the first | Two years | Double salpingo-oophorectomy | Right and left | Both tubes had very larger than a sacrosalpinx; pedunculated, flat and adherent to intestines, pelvic wall and omentum; lumina filled with soft encephaloid tumors; metastatic nodules beneath serosa; at necropsy, a papillary tumor on diaphragm growing in liver | Papillary alveolar carcinoma | Died 3 days postoperative from sepsis |
| 59. | Ponyó and Diner (58, 67) | 50 | Three, the last 30 years ago; menopause at 51 | Egg-sized tumor in right lower part of abdomen which constantly grew larger and gave pain; thin odorless bleeding 1 year ago; urgency and dysuria | Large cystic tumor extending to epigastrium on right side and sausage-shaped tumor, size of a fist, to left of cyst | Three years | Right salpingo-oophorectomy | Right | Right tube sausage-shaped, showing nodules on serosa and entire lumen filled by a tumor; abdominal ostium closed; right ovary converted into a very large cyst | Papillary alveolar carcinoma | Well 13 years postoperative |

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|------------------------------------|--|--|---|--------------|--|----------------|--|---|--|
| 60. Stolk..... (178) | Five children; regular; profuse | Abdominal pain and fever in second pregnancy; for 8 months severe pulling pains in abdomen | Hard, nodular tumor, larger than a fist, to the right and behind cervix | Eight months | Radical pan-hysterectomy | Right | Right tube enlarged, ampulla dilated and filled with cauliflower, medullary, crumbly tumor commencing near uterine end and protruding from abdominal ostium; left adnexa negative; metastases to right ovary and hypogastric and lower lumbar glands; glandular hyperplasia of endometrium | Papillary alveolar carcinoma | Well 4 months post-operative |
| 61. Stolk..... (178) | | | | | | | A tumor in the middle and ampullary portions of the tube | Papillary cylindrical cell carcinoma | Recurrence 11 months post-operative and death 12 months post-operative |
| 62. Bland-Sutton 57 (19) | Sterile; menopause at 49 | Irregular, but frequent discharge of blood | "Felt a fibroid under ether" | | Panhysterectomy | Left | Left tube elongated, the ampulla dilated and filled with a soft growth projecting from the abdominal ostium; metastases to adjacent pelvic peritoneum | Spheroidal cell carcinoma | Recurrence 11 months post-operative and death 12 months post-operative |
| 63. Zangemeister 49 (205) | Premature birth 6 years ago; regular; scant | Two periods of amenorrhea during past year; retention of urine for 1 day | A tumor the size of an emu egg on right side and a cystic tumor the size of an apple on the left; uterus enlarged | One day | Vaginal pan-hysterectomy | Right and left | Left tube elongated, sausage-shaped and containing a mushroom-like projection into lumen; right tube thinner, tortuous, abdominal portion as thick as a little finger and showing papillary masses protruding from the ostium; left ovary cystic; right normal; multiple fibroids and interstitial inflammation of uterus | Papillary carcinoma | Died 3 years postoperative with general carcinosis |
| 64. Zangemeister 47 (205) | Sterile; recently irregular | Irregular bleeding; pains in back; continuous serous-guineous to bloody discharge in past few weeks | Tumor the size of a goose egg to the left of uterus, which was somewhat enlarged | One year | Panhysterectomy; small ovary not removed | Right and left | Left tubo-ovarian cyst, the tubal portion of which was filled with papillary growth; right tube thickened and filled with papillary masses; egg-sized cyst of right ovary | Recurrence showed a myxosarcoma | Recurrence a short while postoperative in vagina |
| 65. Zangemeister 49 (205) | One, 30 years ago; irregular, recently profuse | Pains in back; constipation; incontinence of urine; swelling of abdomen | Tumor, the size of a child's head, to left of uterus | Nine months | Double salpingo-oophorectomy | Right and left | Left tube enlarged, retort-shaped and filled with tumor masses; abdominal ostium closed; right tube thickened, tortuous and the seat of a diffuse growth in the median and abdominal portions; abdominal ostium closed; left ovary cystic; metastases to parietal peritoneum and serosa of uterus | Papillary alveolar carcinoma | Death 7 months later with large recurrences and implantations in scar |
| 66. Borgna..... 40 (23) | Three, the last 13 years ago; regular | Slightly purulent discharge; pains in lumbosacral region | Tumor in left fornix extending to level of anterior superior iliac spine; poorly nourished | Ten months | Double salpingo-oophorectomy | Right | Right adnexa formed a mass the size of a hen's egg composed of the tube which was filled with a soft, friable, cauliflower tumor and a small cystic ovary; left intraligamentous ovarian cyst | Papillary alveolar carcinoma | |
| 67. Von Franqué Morinaga (98, 124) | One child, two abortions; regular | Irregular menses; metro-rhagia and partly bloody and watery discharge; pains in lower part of abdomen, especially on left side | Elongated tumor on right side connected with one the size of an orange in front of the sacrum; uterus enlarged and containing soft masses on sounding | Three years | Curettage; panhysterectomy | Right and left | Left tube rapidly enlarged to fist-sized, retort-shaped ampulla with closed ostium; lumen filled with white, medullary, papillary growth; right tube half as large, retort-shaped, and containing dirty blood-red fluid and tumor particles; in abdominal portion, a few small papillary excrescences and in the middle portion, they filled the lumen entirely; uterine myomas and remnants of superficial growth | Papillary alveolar carcinoma of both tubes; uterine ostium of left tube obliterated by old adenocarcinoma of uterus | |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menstruation | Symptoms | Physical | Duration | Operation | Side | Macroscopic | Microscopic | Course |
|-----|--------------|------------|---|---|--|---------------------|---|----------------|--|------------------------------|--|
| 68. | Buissard (5) | 48 | One, 29 years ago; regular up to present illness; menopause at 47 | Irregular menses; dysmenorrhea; pains in abdomen; pale yellowish discharge; swelling of abdomen; frequency of urination with some dysuria | Mass adherent to uterus | Two years | Left salpingo-oophorectomy | Left | Greatly dilated ampullary portion containing a papillary growth the size of a golf ball; left ovary containing a cyst the size of a small coconut; right adnexa looked normal | Carcinoma | Well 26 months post-operative |
| 69. | Danzel (39) | 47 Married | Two children; regular | Trauma to abdomen 2 years ago; pains in back of abdomen onset, persisting with variable intensity and radiating to thighs; abundant leukorrhoea | Uterus enlarged; posterior cul-de-sac distended, hard and tender | Five months | Panhysterectomy | Right | Right tube size of a pudding and looked like a pyosalpinx; abdominal ostium closed and contained serous fluid and reddish vegetations most abundant in pars externa; left hydrosalpinx; metastases to right ovary; cystic left ovary; fibroid uterus | | Recurrence 2 months post-operative with symptoms of intestinal obstruction due to rectal and perirectal metastases |
| 70. | Lwow (115) | 50 | Two children; menopause at 44 | Bloody discharge and pain.. | Left tube hard, slightly tender and the size of a sausage; uterus somewhat enlarged and tender | Six months | Vaginal hysterectomy | Left | Ostium of left tube enlarged and fringed with small reddish papillary masses | Papillary carcinoma | Recurrence 6½ months post-operative |
| 71. | Roche (131) | 44 | Two children; regular | Metrorrhagia and pains in lower left part of abdomen | | "For some time" | Hysteromyectomy; double salpingo-oophorectomy | Left | Both tubes enlarged, cystic and brownish red; walls thin and tense; in left tube, a cancerous growth the size of a small orange | Carcinoma | |
| 72. | Pelham (136) | 44 Married | Three children; 3 abortions, last 29 years ago; pelvic inflammation after abortion and reddish discharge between periods after last one | Pains in abdomen, especially on left side; feeling of fullness; fever; while under observation, a profuse metrorrhagia, with chill, temperature, hiccup and nausea | Indefinite tumor on right side; ascites; marked anemia | Two to three months | Double salpingo-oophorectomy | Right and left | Right tube the size of a fist, thickened, tortuous and containing several walnut to plum-sized papillary nodules; abdominal ostium closed; left tube smaller and dilated at abdominal end from which a tumor mass protruded; lumen filled with papillary excrescences; right ovary atrophic and cystic; dark colored ascitic fluid | Papillary alveolar carcinoma | Recurrence 1 year post-operative |
| 73. | Pelham (136) | 43 | One abortion 10 years ago followed by peritonitis; regular | Frequent "peritonitis"; profuse, watery, at times bloody, discharge for 3 months; cramplike pains, increase in discharge and dysuria for 2 weeks; became well under treatment but recurrence 9 months later | In right and posterior fornix a partly cystic tumor reaching to lateral pelvic wall; in left fornix an oval cystic tumor | Three months | Right salpingo-oophorectomy; and left salpingectomy; resection of omentum | Right | Right tube thickened, tortuous, and containing a cherry-sized, pedunculated nodule 2 cm. from the uterine end; abdominal ostium open; left tube greatly enlarged, sausage-shaped and containing a small amount of reddish, slightly turbid fluid; whole inner surface covered with necrotic papillary growths; abdominal ostium closed; right ovary normal; metastases to omentum and peritoneum | Papillary alveolar carcinoma | Recurrence 6 months post-operative |
| 74. | Briggs (26) | 50 | Sterile; regular; occasional clots and intermenstrual discharge | Swelling of abdomen associated with pains in lower part of abdomen | Large cylindrical tube on right side, and a smaller irregularly outlined appendage on left side; ascites | Two months | | Right | Right tube enlarged, right ovary normal; metastases to left ovary, wall of left tube, intestines, parietes, and omentum | Cancer | Recurrence 2 months post-operative |

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| 75. Anufrief..... (11) | 51 Married | One, 33 years ago; regular; profuse; menopause at 49 | Pains in lower part of abdomen, lumbar region and left leg; dysuria | Cystic tumor the size of a child's head, and the left uterine tube thickened; right tube, size of an apple, in front of uterus; enlarged inguinal glands; poorly nourished | Four months | Hysterectomy; left salpingo-oophorectomy; right salpingectomy | Right and left | Left tube sausage-shaped, emptied into a subvaginal cyst, containing bloody fluid and containing a large growth confined to the tube; right tube dilated and containing a large marked papillary tumor; enlarged myoma and two polyp in uterus | Papillary alveolar carcinoma; fibrosis | Recurrence 4 months post-operative; left inguinal glands enlarged |
| 76. Tomson..... (186) | 37 | Recently irregular | Irregular metrorrhagia and purulent discharge; later accompanied by severe pain in abdomen; right tuboplasty and left tube fixed to abdominal wall 8 years ago | Resistant in small pelvis; hernia of clatrix | More than three months | Excision of upper part of left tube | Left | Left tube the seat of a new growth; right adnexa normal | Atypical proliferation of epithelial cells | Recurrence 2 months post-operative |
| 77. Bland-Sutton (90) | 49 | | | | | | Left | Tube looked like a paramp; ostium sealed; uterine fibroids | | |
| 78. Cullingworth (30) | 41 Married | Sterile; profuse, regular; menorrhagia and metrorrhagia 3 years ago | Almost continual pelvic discomfort; constant increasing watery, sometimes sanguinous, frequently offensive, discharge; urinary frequency | Fibroid uterus diagnosed 3 years ago; fistulae in right posterior quarter of pelvis; distulous opening in anterior wall | Two years | | Right and left | Right tube enlarged and its abdominal ostium blocked by a solid adherent growth presumably in connection with rectum; left tube sausage-shaped and filled with a soft, cancellatoid growth; metastases to left ovary | Indicating papillary carcinoma | |
| 79. Schenek..... (165) | 53 | Four children; menopause at 50 | Pain in lower part of abdomen associated with thin charge | Mass in left fornix..... | Two years | Left salpingo-oophorectomy | Left | Tube filled with a new growth; distal end dilated; no metastases | Adenocarcinoma | Well 3 years post-operative |
| 80. Hare..... (81) | 29 Married | Sterile; regular; scanty; dysmenorrhea | Sterility | | | Panhysterectomy in 2 stages | Right and left | Tubes thumb-sized at fimbriated ends; ovaries cystic | | |
| 81. Macnaughton (114) | | | | | | | | Tube formed an oval, lobulated mass enclosing a new growth which had broken through the wall in places | Spheroidal cells arranged in columns and connective tissue masses | |
| 82. Rollin..... (135) | 46 Married | One, 18 years ago followed by pelvic inflammation; regular; dysmenorrhea | Pelvic inflammation 12 years ago; watery, tea-colored, odorless, profuse discharge associated with hypogastric pains; dysuria; constipation | Cystic mass in right fornix, rising above the groin; on left side a smaller, tender mass; uterus anteverted and fixed | One year | Panhysterectomy | Right and left | Right tube the size of an orange and left of a tangerine; both filled with chocolate-colored fluid and cauliflower-like vegetations arising from the mucosa; ovaries normal | Epithelioma metatypique | |
| 83. Cullen..... (33) | 55 | | Metrorrhagia; great pain on defecation | Mass on right side..... | "For months" | Radical with resection of omentum and rectum | Right | Extension to peritoneum of pelvic floor, both ovaries and to rectum; extensive metastases to omentum | Papillary alveolar carcinoma | Died 6 months post-operative |
| 84. Pompe Van Merdervoort (144) | 45 | One child | Pains in lower abdomen.... | Marked ascites | One month | | Right and left | Bilateral cystic adnexal tumors; tubes thickened; papillary ovarian tumors? | | |
| 85. Kettler..... (94) | 50 | Two children; regular; menopause at 42 | Severe sticking pains in entire abdomen which gradually ceased after discharge of watery, slightly blood-tinged fluid; swelling of abdomen also diminished; similar attack 2 weeks later | | Ten weeks | | Right | Right tube markedly lengthened and dilated at the abdominal end to the size of a finger; abdominal ostium open; many small pea-sized nodules on pelvic peritoneum; ascites | Carcinoma | Free fluid in abdomen 11 days post-operative |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menstruation | Symptoms | Physical | Duration | Operation | Side | Macroscopic | Microscopic | Course |
|-----|-----------------------------|-----|---|--|--|---------------------|---|----------------|--|---|---|
| 86. | Orthmann..... (133, 134) | 49 | Regular; menopause at 48 | Severe pressure on bladder and rectum; severe constipation and sacral pains | Soft, round cystic tumor, size of child's head to left of uterus which burst during examination | Three months | Left salpingo-oophorectomy | Left | Left tube tortuous and communicating with a large ovarian cyst; beginning 3 cm. from uterine end, the lumen filled with a papillary growth; cyst free except at one point, opposite the tubal orifice | Papillary alveolar carcinoma | Recurrence 9 months and death 1 year postoperative with general carcinoma |
| 87. | Orthmann..... (134) | 53 | One, 31 years ago; 1 abortion 30 years ago; menopause at 43 | Bilateral-staro operation 3 years ago; for 3 to 4 weeks foul yellow discharge; indefinite pains in left part of abdomen and sacrum; burning on urination | Incarcerated umbilical hernia; indefinite resistance in right fornix and pouch of Douglas | Three to four weeks | Double salpingo-oophorectomy; hysterectomy | Right and left | Right tube, papillary alveolar carcinoma in an hydrosalpinx; left tube; incipient carcinoma | Right tube, papillary alveolar carcinoma in an hydrosalpinx; left tube; incipient carcinoma | Recurrence 5 to 6 months postoperative |
| 88. | Zumbusch..... (206) | 43 | Married | Progressive abdominal enlargement; diarrhoea of liver suspected | Tumors to both sides of uterus; ascites | Five months | Double salpingo-oophorectomy | Right and left | Both tubes greatly dilated and filled with a vascular, soft growth; metastases on serous coat, uterus and parietal peritoneum and salpinx | Alveolar carcinoma | Ascites 3 months postoperative |
| 89. | Fehling..... (83) | 60 | Sterile; menopause at 32 | No discharge; abdominal pains, chiefly on right side | | Some weeks | | Right | Bilateral carcinoma with hydrosalpinx | | Well 11 months postoperative |
| 90. | Tydat..... (183) | 56 | Sterile | Gonorrhea 14 years ago; recently leukorrhoea; attack of acute abdominal pain 2 months ago | Tumors in both fornices, the right rising to the iliac fossa | Nine months | Panhysterectomy; resection of pelvic peritoneum | Right and left | Both tubes formed tumors bearing exuberant masses of malignant papilloma and dark fluid; metastases to pelvic peritoneum; after operation, bladder perforated by growth | | Death from recurrence 13 months postoperative |
| 91. | Bertino..... (18) | 48 | One, 23 years ago; regular; menopause at 46 | Profuse, white discharge; enlargement of abdomen; pains in right lower quadrant; debility; constipation | Mass the size of a child's head in anterolateral fornix extending 2 inches above pubis | Four months | Right salpingo-oophorectomy | Right | Tube very much dilated; new growth attached to base of tube; pinkish vegetations; ovary free; ascites | Papillary alveolar carcinoma with invasion of ovarian cortex | Well 1 month postoperative |
| 92. | Kundrat..... (101) | 47 | One abortion 26 years ago; regular; profuse | Tumor in abdomen noticeably larger in past 2 months; bladder and rectal difficulties | Round, hard, smooth tumor in abdominal cavity; on right side of small pelvis a fixed nodular tumor | Two years | Panhysterectomy | Right | Right tubo-ovarian cyst; tumor like wet moss commencing in middle of uterine portion; ampulla filled with chocolate-colored fluid; pea to hazelnut excrescences on cyst wall just beyond junction; left hematosalpinx; left ovary cystic; many small metastases to pelvic peritoneum | Papillary alveolar carcinoma; endometritis diffusa | Died 1½ years postoperative active with cachexia |
| 93. | Kundrat..... (101) | .. | | | Beginning neoplasm of portio vaginalis; to left of uterus a tumor the size of a fist | | | Right and left | Left tubo-ovarian cyst, the tube being filled with a papillary growth and a few mushroomlike nodules on inner wall of cyst; right tube dilated and the seat of a papillary growth the size of a hazelnut; metastases to right ovary; uterine polyp | Papillary carcinoma; metastases to right ovary and cervix | |

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| 94. Martin..... 56 (117) | Three children | Swelling of abdomen; at times pains | Large, partly cystic tumor on right side extending a handbreadth above navel | Nine months | Right salpingo-oophorectomy | Right | Tube sausage-shaped and opened into an ovarian cyst; papillary new growth in outer portion of tube | Carcinoma | Died of septic peritonitis |
| 95. Dandekl..... 44 ? (37) | One, 22 years ago; 1 labor; regular | Severe pelvic inflammation 13 years ago; severe pain in right side and sacro-pelvic region; under observation 1 year; catamenial flow, attacks of pain, yellowish watery discharge and vomiting | Tumor the size of a fist in the right fornix; mass the size of a hen's egg in left fornix | Two months | Right salpingo-oophorectomy; left salpingectomy; hysterectomy | Right and left | Outer portion of right tube dilated into a large cyst containing yellow serum and foil of medullary papillomatous masses; abdominal os-tium closed; left tube enlarged to size of a pigeon's egg near the uterine insertion | Papillomatous adenocarcinoma; endometritis diffusa | Well 6 months postoperative |
| 96. Orthmann.... 51 (135) | Two children; lately profuse, irregular and painful | Severe pains in lower part of abdomen | | Six weeks | | Right | Right tube completely converted into a solid tumor; left sacrosalpinx polyp; multiple fibroids; uterine serosa; | Squamous cell carcinoma; chronic sal-plangitis | Recurrence 3 months post-operative |
| 97. Saretsky..... 40 (100) | Irregular | Vaginal discharge for over 20 years; at first leukor-rhea, then serous and ultimately profuse, periodic, watery; pains in iliac regions | | Many years | Panhysterectomy | Left | Left tube greatly dilated and filled with malignant papillomatous growths; right adnexa and left ovary negative; subserous uterine fibroid; metastatic nodule in broad ligament | | |
| 98. Danel..... 49 (40) | One, 20 years ago; regular | Pains in left side of abdomen increased at time of menses; menorrhagia and irregularity of periods; profuse watery discharge; emaciation | Hard tumor reaching half way up to umbilicus | One year | Double salpingo-oophorectomy; left ovary partially removed; exploratory 9 months later | Right and left | Left tube the size of an index finger and filled almost entirely with reddish-white growth bathed in a mucoid fluid; right tube the size of a pudding and filled with a similar growth; right ovary cystic and the size of a small apple | Papillary carcinoma | Generalized carcinoma 9 months post-operative |
| 99. Amann..... 60 (4, 29) | Two children and 1 abortus | Urinary difficulties | | | Panhysterectomy | Right and left | Papillary tumors of both tubes; metastases to ovaries, omentum, intestine and stomach | Papillary carcinoma | |
| 100. Schauenstein 42 (164) | Sterile; regular | Irregular metrorrhagia; rapid enlargement of abdomen; no pain or discharge | Large tumor filling pouch of Douglas and rising out of pelvis on right side | Three months | Panhysterectomy | Right | Right tube larger than a fist, shaped like a tobacco pipe and adherent to posterior wall of cervix; in dilated ampulla, necrotic masses and crumbly, encysted excrecences; left hydrosalpinx; both ovaries negative | Papillary alveolar carcinoma | Whereabouts unknown |
| 101. Kehr..... 57 (93) | One, 33 years ago; menopause at 48 | Pains in both sides of lower part of abdomen; profuse, at times blood-tinged, discharge | Cystic tumor, as large as a fist, on right side in pouch of Douglas; plum-sized tumor on left side; tumors increased in size while under treatment | Three months | Panhysterectomy | Right | Right tube dilated, elongated, club-shaped; abdominal os-tium closed; part abdominalis filled with a crumbly neoplasm; carcinomatous masses on isthmus; and in region of right ovary; infiltration of right parametrium; left hydrosalpinx; metastases to bladder, uterus, transverse colon, and to both ovaries | Papillary alveolar carcinoma | Recurrence 5 weeks; death 3 months post-operative |
| 102. Gemmell..... 45 (73) | Sterile; regular; at first profuse, now scant | Free white discharge which later became profuse, watery, yellowish and offensive; pains in abdomen, at first in right iliac region and later mainly on left side; swelling of abdomen; loss of weight | Hard, knobby mass almost filling the true pelvis and extending above Poupart's ligament on left side; right adnexa size of hen's egg | One year | Double salpingo-oophorectomy; left ovary partially removed | Left | Left tube sausage-shaped, distended and containing considerable pus and papillary masses; right hydrosalpinx; ovaries normal | Papillary carcinoma | Well 8 months postoperative |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menstruation | Symptoms | Physical | Duration | Operation | Side | Macroscopic | Microscopic | Course |
|------|-------------------|-----|---|--|---|--------------|------------------------------------|-------|---|---|---|
| 103. | Mérid | 41 | Sterile; menopause at 25 | Severe pains in pelvis associated with metrorrhagia alternating with leukorrhea | Cystic tumor in region of right adnexa | Nine months | Panhysterectomy | Right | Right tube converted into large cyst containing bloody fluid and fleshy, velvety, papillomatous growth; suppurating cyst of right ovary; no metastases | Papillomatous epithelioma | Well 6 months postoperative; killed in accident 8 months later |
| 104. | Everke | 46 | Two, the last 12 years ago | Recent bloody discharge; early in marriage, profuse purulent discharge | In right parametrium, a tumor as big as a fist | A few months | | Right | Enlarged right tube pushing into parametrium and adherent to sigmoid | | 21 months postoperative operated for cancer of stomach; died 3 years post-operative |
| 105. | DeLaunay | 52 | Menopause at 48 | Enlargement of abdomen... | Cystic tumor extending above umbilicus | Two years | Left salpingectomy and ovariectomy | Left | Large ovarian cyst; left tube as large as a thumb with thickened walls and projecting longitudinal folds of mucosa | Incipient carcinoma | Recurrence 4 months, and death 6 months postoperative |
| 106. | Norris | 27 | Two children; regular | Pelvic peritonitis after birth of last child and since then dull pains in lower part of abdomen; lumbar and sacral backache; considerable yellowish, at times foul, discharge which in past 5 months had become more profuse, watery and occasionally brownish | Inflammatory masses to both sides and behind uterus | Four years | Panhysterectomy | Right | Right tube retort-shaped and containing watery, blood-stained fluid and grayish, accephaloid, papillary growth in ampulla; abdominal ostium closed; left hydrosalpinx; perioophoritis | Papillary alveolar carcinoma; chronic salpingitis | |
| 107. | Lorrain | 39 | Two abortions; 2 children, last with retained placenta and dilation and curettage; irregular; amenorrhea and metrorrhagia | Pains in lower part of abdomen during menses; scanty menses, the last accompanied by fetor | Tender left ovary..... | Ten months | Left salpingo-oophorectomy | Left | Left tube larger and longer than normal; tumor, the size of a lentil, in upper border of midportion of tube; left ovary sclerotic and cystic | Typical epithelioma | |
| 108. | Gosset | 44 | Three, the last 12 years ago; regular | Profuse, watery discharge between periods; no pain; progressive swelling of abdomen for 1 year | Smooth, firm tumor in left iliac fossa | Three years | Panhysterectomy | Left | Left tube sausage-shaped; medullary growth in tubal wall not arising from mucosa; right hydrosalpinx; metastases to great omentum | Perithelioma, possible angiosarcoma | |
| 109. | Caraven and Lerat | 54 | One abortion 30 years ago; regular; menopause at 53 | Abundant, watery discharge, pink at first, then colorless; abdominal pains on left, side with an acute attack 14 days ago which radiated to lumbar region and was associated with nausea | Uterus enlarged; hard mass in left cul-de-sac | Six months | Salpingectomy | Left | Lardaceous tumor in left tube..... | Papillary alveolar epithelioma | Died 1 year postoperative with general carcinosis |
| 110. | Leclae | 48 | Three children and 1 abortion; menses obscured by hemorrhages | Metritis with peritonitis and hemorrhages following abortion; metrorrhagia at first intermittent, now almost continuous | Mass filling pouch of Douglas and continuous with a hard tumor extending to the umbilicus | Two years | Panhysterectomy | Right | Right tube dilated, tortuous, the size of fist, and filled with a medullary, seminecrotic, rose-colored tumor; left hydrosalpinx; abdominal ostium closed; right ovary cystic; metastases to left ovary; myomas of uterus; metastases to cervix | Papillary alveolar carcinoma | Well 10 months postoperative |

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| 111. Benthin..... 40 (17) | One, 18 years ago; regular | Profuse, brownish discharge before and after menses, which had a foul odor; pains in region of umbilicus and right lower quadrant | Uterus displaced backward and to the left by an elastic tumor | One year | Panhysterectomy | Right | Right tube retort-shaped and its ampulla as large as a fist and filled with a reddish-brown cauliflower growth; abdominal ostium closed; chronic salpingitis of left tube; left ovary cystic; metastases to right ovary and broad ligament | Papillary alveolar carcinoma | Well 5 years postoperative |
| 112. Boxer..... 62 (25) | One, 30 years ago; regular; profuse; menopause at 51 | Meat-water, foul discharge, now more purulent; cramp-like pains in right lower part of abdomen radiating to right thigh, sacrum, and to rectum, with tenesmus; loss of weight | Resistance behind and to right of uterus | Six months | Panhysterectomy (radical) | Right and left | Right tubo-ovarian cyst; tube retort-shaped and containing a crumbly, hemorrhagic, papillary tumor commencing in the isthmus and almost completely filling the ampulla; a few excrescences on cyst wall; left tube somewhat dilated, tortuous, the abdominal end distended, and the lumen filled with brownish masses; abdominal ostium closed; small myoma and polyp of uterus | Papillary alveolar carcinoma | Died a few months postoperative |
| 113. Boxer..... .. (25) | | | | | | Right and left | Bilateral tubo-ovarian cysts; the lumina filled with crumbly, grayish-white tumor masses; walls of cysts contained a few excrescences | Papillary alveolar carcinoma | |
| 114. Penkert..... .. (139) | | | | | | Right | Metastases to both ovaries..... | Alveolar carcinoma containing sarcomatous tissue | |
| 115. Balesch and Baabe..... 47 (13, 146) | One, 28 years ago; irregular and profuse in past 3 years | Continuous metrorrhagia of varying intensity | A tumor, the size of a child's head, to left of uterus and one the size of a fist, in region of right adnexa | Three years | Panhysterectomy | Left | Left tubo-ovarian cyst; tube sausage-shaped and filled with a papillary tumor and crumbly masses; wall of the cyst contained a few nodules; right hydrosalpinx; cystic right ovary; small papillary growth of uterus | Papillary alveolar carcinoma; metastases to abdominal wall; left ovary and uterus | 6 months postoperative, metastases to abdominal wall; excised, but recurred 6 months later |
| 116. Rossinsky.... 42 (154) | Three children and 2 abortions; regular | Gonorrheal pelvoperitonitis; abdominal pains; meat-water discharge; loss of weight | | | Left salpingo-oophorectomy | Left | Tube, pear-shaped, cystic and filled with a papillary growth; ambricated end atresic; tubo-ovarian cyst with a few small carcinomatous areas; palpable supraclavicular gland | Carcinoma cylindro-papillary cellular | 3 months postoperative supraclavicular gland size of an apple excised; showed carcinoma |
| 117. Doran..... 60 (46) | One child; menopause at 47 | Regular flow of blood returned 3 years and ceased 6 months ago; abdominal swelling, 5 months; pain in right side of abdomen; dysuria; suppurating cavity in posterior fornix opened a month ago | Tumor in left fornix and pouch of Douglas extending nearly to ensiform | Three years | | Left | Large tubo-ovarian cyst filled with several pinns of reddish-brown fluid; papillomatous masses filling tube and invading wall; a few patches in cyst; metastases to serosa of uterus and pouch of Douglas | | Died 3 years postoperative with general carcinoma |
| 118. Tate..... 52 (182) | Three, the last 17 years ago; menopause at 48 | Yellowish, blood-stained discharge and some pain and discomfort in pelvis; following an accident, fever, pains in lower left part of abdomen and vomiting | Cystic swellings as large as hens' eggs to both sides of uterus, which is retroverted; tenderness in hypogastrium and left iliac region | Two years | Double salpingo-oophorectomy; left ovary partially removed | Right | Right tube elongated, tortuous, thickened, and cavity filled with a soft, friable growth; left pyosalpinx | Glandular carcinoma | Well 37 months postoperative |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menses | Symptoms | Physical | Duration | Operation | Side | Macroscopic | Microscopic | Course |
|------|-----------------------|-----|---|--|---|---------------------|---|----------------|--|-----------------------------------|---|
| 119. | Tate..... (182) | 44 | Sterile; metrorrhagia | Pains in back and left hip; three febrile attacks | Hard, nodular mass adherent to lateral wall and filling the right side of pelvis | Three months | Double salpingo-oophorectomy; resection of omentum | Right and left | Right tube tortuous, thickened, with plaques of new growth on walls; lumen filled with caseous material; mucosa absent; left tube, end of a horn, showed similar plaques and contained dermoidlike material; metastases to right ovary, omentum and appendix | Columnar cell carcinoma | |
| 120. | Spencer..... (175) | 64 | Multipara; regular; menopause at 48 | "Fallen womb" for 40 years; greenish, offensive discharge, bloody for past 5 months; small growth removed from vagina 4 months ago | Small red growth in posterior vaginal fornix; thickening of left appendages | Five months | Panhysterectomy | Left | Outer half of tube the size of a pigeon's egg; extreme end distended by fluid, but not affected by growth; metastases to vagina | Columnar cell carcinoma | |
| 121. | Spencer..... (175) | 35 | Virgin; irregular | Noticed a lump in abdomen which has increased in size of late; pains especially on left side; slight leukorrheal discharge before flow | Tumor rising above pubis and fixed in iliac fossa; hard tumor surrounding and continuous with cervix | Eighteen months | Left salpingo-oophorectomy | Left | Left tube full of a brittle growth at one point perforating the wall; the latter completely destroyed except at uterine end; left ovary cystic; myomas of uterus; metastases to adherent intestines; ascites | Columnar cell carcinoma | Recurrence in incision a short time postoperative; active; death 1 year later |
| 122. | Spencer..... (175) | 53 | One child, 3 abortions; regular; menopause at 48 | Progressive swelling of abdomen; frequency of urination; pains especially in epigastrium; swelling of ankles | Hard tumor, as large as a fist, to left of retroflexed uterus; cystocele; marked ascites | Six weeks | Left salpingo-oophorectomy; resection of broad ligament | Left | Left tube rapidly enlarges to osium where growth had broken through wall; tube completely filled with a yellowish-white tumor and perforated by it in two places; invasion of broad ligament | Papillary columnar cell carcinoma | Recurrence 3 months postoperative on exploratory, extensive metastases |
| 123. | Legg..... (167) | 45 | Regular | Increasing colicky pains in left iliac and lumbar regions accompanied by bloody discharge; swelling of abdomen | Tumor extending into right iliac fossa and nearly to navel on right side; smaller tumor on left side; uterus apparently enlarged | Twenty-eight months | Double salpingo-oophorectomy | Right and left | Left tubo-ovarian cyst; lumen of tube filled with a yellowish-white, solid tumor; a few milary nodules on serosa; right tube retort-shaped, dilated and containing a papillomatous growth 2 cm. from uterine end; right ovary not distinguishable | Malignant papilloma | Well 3 years postoperative |
| 124. | Ballin..... (126) | 47 | Regular | Sparse, thin, blood-tinged discharge; attack of pain in abdomen with fever lasting 3 weeks | Mass as large as a fist in front of and to left of uterus; one, the size of a walnut, on right side; rapid increase in size of right-sided tumor during acute attack and gradual growth of left tumor | Ten months | | Left | Right hydrosalpinx; ovary normal.. | Papillary adenocarcinoma | |
| 125. | Cullen..... (34) | 46 | One miscarriage 28 years ago; recently irregular dysmenorrhea | Pains in right iliac region 2 years ago and for past year in left side, radiating to knee; recently, profuse discharge which became bloody and foul in past year | | More than one year | | Right and left | Right tube sausage-shaped and filled with a granular, arborescent growth; left tube smaller and containing a similar growth | Papillary alveolar carcinoma | Recurrence |

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| 126. Koenig..... (186) | | | | | Left | Panhysterectomy; incomplete removal | Left | Left tube very large and semicyclic; pelvic peritoneal metastases and papillary growths on surface of uterus and adnexa; right hydrosalpinx | | Recurrence 1 year postoperative with compression of rectum; reovaginal fistula |
| 127. Montgomery..... (123) | | | | | Right | Right salpingectomy; later panhysterectomy | Right | A tumor, like a fibroid undergoing fatty degeneration, at outer end of right tube; tuberculoma of left tube; interstitial fibroid of uterus | Cylindrical cell carcinoma | Well 8 months postoperative |
| 128. Tweedy..... (188) | | | | | Right | Right salpingo-oophorectomy and left salpingectomy in two stages | Right | Fungating mass adherent to both ovaries and intestines; mass of organized blood clot in cul-de-sac | Carcinoma | |
| 129. Vignard..... (193) | | | | | Left | Double salpingo-oophorectomy | Left | Left tube dilated and filled with fluid and vegetations; metastases to left ovary and a few vegetations on outer surface of right tube; ascites | Cylindrical cell epithelioma | |
| 130. Weinbrenner..... (199) | | | | | Left | Removal of tube and uterus | Left | Tube at abdominal end twice the thickness of a thumb and filled with a medullary tumor invading the ovary; abdominal ostium closed; right hydrosalpinx; uterine fibroid | Papillary alveolar carcinoma | |
| 131. Maiss..... (115) | | | | | Left | Vaginal panhysterectomy | Left | Left tube formed a peach-sized sacrosalpinx containing serosanguinous fluid and detritus; abdominal ostium closed; inner surface covered with papillary excrescences; right adnexa negative | Papillary alveolar carcinoma; chronic salpingitis | |
| 132. Meyer..... (120) | | | | | Left | Double salpingo-oophorectomy | Left | Left tube greatly dilated and contained a papillomatous tumor | Carcinoma | Died 10 days postoperative with peritonitis |
| 133. Wesinger..... (202) | | | | | Right | Left salpingo-oophorectomy; right salpingectomy | Right and left | Both tubes retort-shaped and filled with a tumor-like balled bone marrow; abdominal ostia closed; left unilocular cyst of ovary | Papillary alveolar carcinoma | Metrorrhagia 2 months postoperative; curettings; no cancer |
| 134. Von Franqué..... (71) | | | | | Left | Panhysterectomy | Left | Left tube as thick as a finger, tortuous and filled with grayish-white soft masses; metastatic nodules on serosa; abdominal ostium closed; right tubal wall markedly thickened and the abdominal ostium closed; both ovaries apparently normal; fibroid uterus, metastases to serosa of uterus and to intestines | Old chronic tuberculous of both tubes; polypoidous carcinoma in middle portion of left tube; a few milary tubercles in left ovary | Recurrence 3 months postoperative and death some-what later |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menses | Symptoms | Physical | Dura- tion | Operation | Side | Macroscopic | Microscopic | Course |
|------|---|--------------------|--|--|---|-------------------|--|----------------------|---|---|--|
| 135. | Karakos..... (92) | 55 | Two children | Urinary difficulties | | | | Left | Left tube greatly enlarged; right ad- nexa, left ovary and uterine end of left tube negative | Individual cells like round and spindle cell sarcoma, but arranged like carcinoma | |
| 136. | Eglinton.... (62) | 47 | Two children; menopause at 44 | Gonorrhea ?; fetid, watery, often blood-streaked dis- charge; frequency and in- continence in past year; loss of weight | | Thirteen years | Left salpingo- ophorectomy | Left | Left tube retort-shaped, tortuous; the outer end dilated to the size of a pigeon's egg and filled with a fri- able, shaggy mass | | |
| 137. | Alchel..... (1) | .. | | | | | | Right and left | Both tubes completely closed and intact; both ovaries normal; in- flammatory proliferation on peri- toneum enclosing clumps of en- cer cells | Carcinoma | |
| 138. | Kaarsberg.... (98) | 40 | | Bleeding | | | | Left | Carcinoma polypusoid of left tube; bilateral chronic salpingitis; fibro- ma uteri | | |
| 139. | Beckmann.... (16) | .. | | | | | Vaginal pan- hysterectomy | Right and left | Both tubes mobile with spindle-like enlargements of middle portions; abdominal ostia open; uterus en- larged and cavity filled with car- cinomatous masses | Adenocarcinoma | Recovery |
| 140. | Von Buhhoff (29) | 50 | Three children; regular; meno- pause at 45 | Pains in left side of abdo- men; feeling of pressure in pelvis and on bladder; loss of weight | Irregular cystic tumor on left side | A few months | Left salpingo- ophorectomy | Left | Left tube enormously dilated and retort-shaped; wall thin as paper and the abdominal ostium closed; ampulla filled with gelatinous masses and a compact tumor the size of a child's head | Papillary alveo- lar carcinoma; metastases to ovary; chronic salpingitis | |
| 141. | Seneert..... (173) | 38 Mar- ried | Two, the last 5 years ago; regular | Pains in abdomen and pelvis radiating to back and loins, recently in form of crises; intermittent, pro- fuse; watery discharge streaked with blood | Hard, fixed, tender mass, the size of an orange, in the right lateral and posterior cul-de-sac | Two years | Panhyster- ectomy | Right | Right tube cylindrical in shape and containing a viscous fluid streaked with blood; lumen filled with caul- flower, papillomatous masses | Papillary carcinoma | |
| 142. | Schottlaender and Kermanner (168) | 43 | One child; irreg- ular and more profuse in past 2 years | Pains in back and both thighs; in last 3 months, obstipation and tenesmus with passage of mucus and blood; loss of weight | Uterus the size of a child's head; cystic tumor in posterior cul-de-sac, to right of which was a nodular, fixed tumor | One year | Radical pan- hysterec- tomy | Right and left | Right tube formed a large tumor at its abdominal end; left tube thick- ened and containing medullary nodule in its wall; extensive adeno- carcinoma and myoma of uterus | Papillary alveolar carcinoma; metastases to both ovaries | Death 2 months months post- operative; at necropsy the car- cinoma filled entire pelvis, breaking into bladder and ileum |
| 143. | Gurd..... (79) | 46 | Five, the last 9 years ago; regular | Weakness and anemia for 4 months; last period de- layed and profuse; pro- fuse, watery, slightly puru- lent discharge of heavy odor in past 2 weeks | Small, firm mass to left of uterus; anemia of uterus; anemia | Four months | Left salpingo- ophorectomy | Left | Tube egg-shaped, firm, smooth and containing a small amount of pur- ulent material and a grayish-pink, friable tumor at its abdominal end | Alveoli composed of spindle and polyhedral cells | |
| 144. | Kubinyi..... (100) | 43 | Four children | Rapid swelling of abdomen.. | Tumor, size of a flat, to right of uterus; ascites; cachexia | Three months | Left salpingec- tomy; resection of omentum | Right | Right tube formed a sausage-shaped tumor; several metastatic nodules in omentum; right ovary, left ad- nexa and uterus negative; ascites | Papillary alveo- lar carcinoma | |

| | | | | | | | | | | |
|------------------------------------|----|--|---|---|-----------------|---|----------------|--|---|--|
| 145. Waner and Teuschlaender (106) | 55 | | Excision of twisted ovarian tumor 3 years ago; obstipation; tenesmus | Cystic tumor in septum rectovaginalis completely filling small pelvis and occluding vagina and rectum | "For some time" | Left salpingo-oophorectomy; curettage of cyst | Left | Left tube tortuous with a nodular, walnut-sized tumor at abdominal end; fimbria plump and thick; near the uterine end, a nodular, subserous growth; metastases to septum rectovaginale | Papillary alveolar carcinoma | "Doing well" |
| 146. Drutmann (40) | 54 | | Indefinite lower abdominal symptoms; blood-tinged serous discharge | Curettings showed carcinoma | Two years | Panhysterectomy | Right | Tubes normal except for a tumor the size of a pea in the intramural portion of right tube; tumor yellow, of the consistency of butter, and looked like a degenerated fibroid; ovaries atrophic; uterine fibroid | Carcinoma of adenomatous type apparently not arising from the mucosa | |
| 147. Einde (53) | 47 | One, 25 years ago; regular; profuse | Pains in lower part of abdomen radiating to sacral region; metrorrhagia; no discharge | Movable, tender tumor in right hypochondrium and in region of uterus, a nodular tumor, both the size of a fist | Five weeks | Panhysterectomy | Right and left | Right tubo-ovarian cyst; tube retort-shaped, tortuous, and containing a yellowish, medullary tumor arising mainly in middle portion; a few small nodules in ampulla and even less in cyst; lumen filled with loose, crumbly masses of tumor tissue; left tube dilated at ampulla to size of walnut and filled with a papillary tumor; abdominal ostium closed; left ovary normal; uterus myomatous, and in right cornu and to a lesser degree all over fundus, small papillomatous growths | Papillary adenocarcinoma; chronic salpingitis; endometritis glandularis | |
| 148. Vest (102) | 56 | One, 20 years ago; regular; menopause at 54 | Gradually increasing tumor in abdomen; loss of weight; frequent urination | No pelvic examination; ascites | Six months | Left salpingo-oophorectomy | Left | Left tube distended and filled with a grayish, granular growth; abdominal ostium closed; large left intraligamentous ovarian cyst; ascites | Papillary carcinoma | Recurrence 2 years and death 4½ years post-operative |
| 149. Vest (102) | 44 | Seven children and 1 miscarriage, the last 13 years ago; menorrhagia for 18 months | Profuse leukorrheal discharge; sharp pains in left lower part of abdomen; frequency and dysuria; loss of weight | Fundus enlarged by a hard, nodular mass attached to it; left adnexa formed mass, the size of a fist; nodular masses throughout pelvis | Two months | Hysteromyectomy; double salpingo-oophorectomy | Left | Left tube markedly distended in its middle and outer portions; abdominal ostium open and projecting from it a grayish-white, spongy, papillary tumor; right ovary normal; metastases to peritoneum and omentum; uterine myoma | Papillary carcinoma | Died 6 months postoperative |
| 150. Vest (102) | 47 | Sterile; regular; getting scant during past year | Increasing fulness of abdomen; weakness and loss of weight; pains in abdomen and legs; vomiting; slight temperature and chilly sensations; constipation | Fundus enlarged; irregular, nodular, pedunculated tumor on left side, the size of a fist; ascites | | Left salpingectomy | Left | Left tube evenly distended, doughy, and filled with grayish-white, putty-like masses attached practically to the entire inner surface of the tube; tumor cauliflower in places; abdominal ostium closed; right ovary normal; metastases to pelvic peritoneum, omentum, intestines; ascites | Papillary carcinoma | Died 9 months postoperative |
| 151. Hoerrmann (83) | .. | | | | | | Right and left | On right side, the tubal carcinoma had broken through into a coil of small intestine | | |
| 152. Lewis (110) | 48 | Eight children; 1 abortion; regular | Gradual growth of tumor in abdomen; slight serous discharge | Ascites; tumor rising a hand's breadth above symphysis and adherent to uterus | One year | Radical panhysterectomy; incomplete | Left | Left tube contained papillary growths; metastases to pelvic peritoneum | Carcinoma papillare | Return of ascites in 3 months |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menses | Symptoms | Physical | Duration | Operation | Side | Macroscopic | Microscopic | Course |
|------|---------------------------|------------|---|---|---|----------------|--|----------------|---|--|---|
| 153. | Lewitsky..... (116) | 50 | Two children; dysmenorrhea for 12 years | Intermenstrual pains; blood-tinged discharge | Like multiple myomas.... | Three years | Radical panhysterectomy | Right and left | Right tube formed a sacculosalpinx, size of a fist, containing papillary growths; left tube formed a tumor size of a plum, and also containing a cancerous growth | Papillary alveolar carcinoma | |
| 154. | Cumston..... (32) | 52 | Two children; menopause at 50 | Acute paroxysmal abdominal pain, especially in left iliac fossa; rose-colored, watery discharge | Oval tumor, size of orange, on left side | Four months | Hysterectomy; left salpingectomy | Left | Left tube formed a pear-shaped tumor filled with dirty, bloody liquid and papillomas; abdominal ostium closed; ovaries atrophic; right tube normal | Papillary carcinoma | Well 7 months postoperative |
| 155. | Lipschitz..... (111) | 44 | Sterile; irregular | Menstrual backache; pains in right side of abdomen; "falling down" feeling; obstipation | Nodular, fixed, retroverted uterus; adnexa not definitely palpable | One year | Panhysterectomy; left ovary only partially removed | Right | Right tube tortuous, thickened and dilated at ampulla to form a hazelnut tumor containing reddish fluid and crumbly, white tumor tissue; abdominal ostium closed; left tube normal; uterine myomas removed | Tuberculous salpingitis; borderline papillary alveolar carcinoma | Reoperated 6 months later; enlarged pelvic glands |
| 156. | Oskar..... (31) | 42 | Normal | Pains in abdomen and lumbar region | Large mass filling left cul-de-sac | Three months | Panhysterectomy | Left | Left tube filled with pus..... | Carcinoma | |
| 157. | Schottlaender .. (167) | .. | | | | | | | Cystic fibro-adenomas of both ovaries; primary carcinoma of one tube | | |
| 158. | Andrews Russel (9) | 55 | Sterile; menopause at 49 | Bloody discharge which later turned to "pure white" | | Fifteen months | | Right and left | Both tubes greatly dilated and filled with papillary growths, especially the right | Papillary carcinoma | |
| 159. | Spencer..... (176) | .. | | | | | | | Tubo-ovarian cyst; growth confined to the ampulla; uterus contained a small fibroid and an adenomyoma | Papillary alveolar carcinoma; extensive keratinization; looks like sarcoma in places | |
| 160. | Barret..... (14) | 46 Married | Sterile | Pains in right iliac fossa.... | Hard tumor in right side of abdomen filling pouch of Douglas and both lateral fornices | Ten years | Panhysterectomy | Left | Right tube extensively tuberculous; left tube lined by tuberculous granulation tissue and toward the outer end, there was a cancerous growth; uterus and ovaries free | Squamous cell carcinoma; extensive keratinization | |
| 161. | Strassmann (179) | 49 | | Severe pains in right side of abdomen | Tumor on right side..... | | Right salpingo-oophorectomy | Right | Isthmus of right tube dilated, larger than an egg and adherent to ovary; ovary cystic | Carcinoma | |
| 162. | Latzko..... (104) | 39 | | Vaginal discharge which in past 5 weeks became blood-tinged and associated with pains in right side of abdomen | Soft tumor, size of fist, to the right, and smaller, denser tumor to left of uterus; amber, serous fluid coming from uterus | One year | Panhysterectomy | Right and left | Right tubo-ovarian cyst as large as a fist; both tube and cyst wall lined with soft, papillary masses; left tube elongated, thin-walled and larger than a thumb; filled with similar papillary growths; abdominal ostium closed | Papillary alveolar carcinoma; metastasis to right ovary | |
| 163. | Thaler..... (184) | 37 | One child; 1 abortion 4 months ago; regular | Following curettage for retained placenta, profuse, watery discharge, progressive loss in weight and attacks of pain in right lower part of abdomen | Uterus, both adnexa thickened, especially the right | Four months | Panhysterectomy; appendectomy | Right | Right tube looked like a hydrosalpinx and contained a papillary tumor in the ampulla, size of child's head; left hydrosalpinx; in uterine cavity, free pieces of tumor tissue | Papillary carcinoma; metastases to right ovary and appendix | |

| | | | | | | | | | |
|---------------------------|--------------------|--|---|--|-----------------|--|-------------------|---|--|
| 164. Frieschmann (166) | 39 | Multipara; profuse and lengthy for past 3 months | Cystosarcoma of left ovary 13 years ago; fever and severe pains in left abdo- men radiating to legs for 8 days; under observation, inflammatory symptoms subsided, and then 4 months later, severe me- trorrhagia | Tender, somewhat mov- able tumor, size of small fist, on right; be- came smaller under ob- servation | Three months | Hysterectomy; right salpingo- ophorectomy | Right | Right tube retort-shaped; ampulla the size of a fist and filled with papillary growths; in uterine por- tion, jelly-like masses; abdominal ostium closed; ovary free | Papillary alveo- lar carcinoma |
| 165. Schweykart (172) | 56 | Two children; last 33 years ago; regular; menopause at 53 | Irregular, slight metror- rhagia; pains in right lower part of abdomen and loss of weight for a few months | Tumor, size of fist, in re- gion of right adnexa | Nine months | Hysterectomy; right salpingo- ophorectomy; left salph- gectomy | Right | Right tube fist-sized, containing a hard, smooth, solid tumor com- mencing 1 cm. from the uterine end; right ovary and left adnexa normal; no metastases | Adenocarcinoma |
| 166. Mantel..... (116) | 73 Mar- ried | Sterile | In sanitarium for dementia senilis; died of pneumonia | Necropsy | | | Left | Left tube enlarged at ampulla to a thumb-sized sac filled with a yellow- ish-red tumor; small right hydro- salpinx; ovaries negative; metas- tases to liver and retroperitoneal glands | Papillary alveolar carcinoma |
| 167. Ruge..... (157) | 53 | One, 35 years ago, then 2 mis- carriages; after the first, peri- tonitis | Urinary retention, urgency, dribbling and nycturia; constipation; attack of bronchitis while under ob- servation | Cystic tumor extending half way to umbilicus and pushing uterus forward | Six weeks | Left salpingo- ophorectomy; nephrectomy | Left | Left tubo-ovarian cyst; encephaloid, papillary tumor beginning and most marked in middle portion of tube where it had penetrated the wall almost to the serosa; cyst free except immediately proximal to the junction with the tube | Papillary alveo- lar carcinoma; chronic sal- pingitis |
| 168. Ruge..... (157) | 52 | Nine children, last 18 years ago; regular; menopause at 51 | Pains in lower part of ab- domen, especially on left side; backache, urinary fre- quency and urgency; swell- ing of abdomen; loss of weight | Marked ascites; doughy tumor, the size of child's head, suprapubic and extending 3 fingerbreadths above the symphysis | Nine months | Panhyster- ectomy; resec- tion of gland | Left | Left tube enormously enlarged, spirally wound and filled in its middle and ampullary portions by a polypoid, grayish tumor; ab- dominal ostium closed; tube in con- tact but not in communication with a large ovarian cyst; right ovary cystic; right tube normal; uterine polyp; ascites | Papillary alveolar carcinoma; lym- phatic metastases in serosa of uterus, in parametrium, iliac glands and solid portion of right ovary |
| 169. Ruge..... (157) | 64 | Three children followed by a miscarriage and peritonitis 36 years ago | Severe metrorrhagia 10 years ago; pains in abdomen; phlebitis a month ago | Tumor, size of a child's head to right of uterus; the left adnexa thick- ened and tender | A few months | Panhyster- ectomy | Right and left | Left tube formed tumor larger than a fist, shaped like a horn, ending in a large sac and containing in its middle and ampullary portions a polypoid, medullary tumor; left tube tortuous, the size of a thumb at the ampulla and containing a solid medullary tumor in isthmus and ampulla; abdominal ostium closed; uterine cavity completely filled with a similar tumor spring- ing mainly from the right side and penetrating musculature dorsally almost to serosa; ascites | Papillary alveolar carcinoma |

Recurrence 5
months post-
operative

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children; Menstruation | Symptoms | Physical | Duration | Operation | Side | Macroscopic | Microscopic | Course |
|------|-----------------------------|--------------|---|---|--|-------------|--|----------------|---|--|-----------------------------|
| 170. | Buge..... (157) | 54 | Sterile; regular; menopause at 47 | Foul, yellowish discharge; pains in lower part of abdomen; frequency of urination; loss of weight | Soft, slightly movable tumor; the size of child's head; to right of uterus, filling pouch of Douglas; a smaller, irregular tumor on the left | Five months | Panhysterectomy; removal of nodules from bladder and pelvic peritoneum; those on sigmoid left behind | Right and left | Right tube rapidly enlarged to end in a cyst the size of two fists; it contained a medullary tumor commencing 2 cm. from the uterine end and stopping abruptly at communication with cyst; latter free except for a few small nodules; left tube tortuous, and size of a thumb at ampulla where it was filled with a medullary tumor; abdominal ostium closed; right ovary atrophic; metastases to left ovary | Papillary alveolar carcinoma | |
| 171. | Moench..... (122) | 51 | One child 20 years ago; regular up to 1 year ago when profuse and irregular; menopause at 50½ | Profuse, white discharge, recently foul; pains in lower part of abdomen at times; loss of weight | Myoma of uterus reaching almost to umbilicus; two tumors posteriorly in small pelvis | One year | Panhysterectomy | Left | Left tube almost as thick as a man's arm, elongated, retort-shaped and filled with clear, serous fluid and a few pieces of white tissue; entire surface covered with wartlike papillae; abdominal ostium closed; right hydrosalpinx; ovaries cystic; myoma of uterus | Papillary alveolar carcinoma | Well 6 months postoperative |
| 172. | Knoop..... (97) | .. | | | | | | Right and left | Bilateral primary carcinoma of tubes with metastases to uterine mucosa | | |
| 173. | Schwartz..... (160, 170) | .. | | | | | | | Tubo-ovarian cyst with three small papillary carcinomas | | |
| 174. | L'Esperance (106) | 35 | | Irregular metrorrhagia; considerable leukorrhea; loss of weight | Fixed, irregular, enlarged uterus; adnexa not felt; curettage showed an atypical plexiform carcinoma | Four weeks | Panhysterectomy | Right | Right tube greatly thickened, dilated and fibria fused; arising from mucosa, irregular, papillary projections occluding lumen in abdominal portion; left pyosalpinx; small fibroid in uterus | Tuberculous salpingitis of both tubes; papillary plexiform carcinoma of right tube with epidermoidization; vascular metastasis to uterus with secondary involvement of a small portion of mucosa | |
| 175. | Phillips..... (142) | 44 Single | Regular | Whitish, foul-smelling discharge; loss of weight; slight pain in lumbar region | Atresia of vagina; tumors to both sides of uterus | One year | | Right and left | | Papillary carcinoma | |
| 176. | Robinson..... (150) | 56 | | Prolapse of uterus..... | Prolapse of uterus; no tenderness or tumors palpable | | Vaginal panhysterectomy | Right and left | Both tubes chronically inflamed; thickened and adherent; abdominal ostium closed; right intraligamentous ovarian cyst; fibromyoma of uterus | Adenocarcinoma | |
| 177. | Barris..... (15) | 55 | Three children, the last 30 years ago; menopause at 52½ | Almost continuous metrorrhagia; loss of weight | Cystic swelling almost filling cavity and displacing uterus to the left | | Panhysterectomy | Right | Right tube distended, smooth, knicked and filled with altered, blood-tinged fluid and papillomatous masses; abdominal ostium closed; several minute nodules on anterior surface of uterus; right ovary enlarged; left ovary normal | Columnar cell carcinoma; metastasis to right ovary | |

| | | | | | | | | | | | | |
|-----------------------------------|----|---------|---|--|--|--------------------|--|----------------|---|--|---|--|
| 178. Rohdenburg (132) | 45 | | | Usual symptoms of adnexal disease | | | | | | Right | Right tube looked like a pyosalpinx; filled with bloody fluid and inner wall rough and covered with papillary growths; left hydrosalpinx; ovaries fibrous and cystic; uterus normal | Papillary carcinoma; metastasis to right ovary |
| 179. Schweitzer, (171) | 53 | Widow | One, 30 years ago; menorrhagia for past 2 years; menopause 5 months ago | Pulling pains in abdomen and sacral region | Adnexal tumor on left side | Nine months | Hysterectomy; left salpingo-oophorectomy | Left | Left tube sausage-shaped, tortuous, as thick as a thumb and filled with a hard, smooth tumor; abdominal ostium open; left ovary normal; right adnexa normal; fibroid | Papillary alveolar carcinoma | | |
| 180. Schweitzer, (171) | 57 | Married | Five children, 1 miscarriage, the last pregnancy 20 years ago; menopause at 48 | Pains in abdomen | Hard, nodular, slightly movable tumor to right of uterus | Six weeks | Vaginal pan-hysterectomy | Right | Right tube formed a fist-sized tumor containing a growth which invaded uterine wall; a cherry-sized, papillary excrescence on abdominal end of left tube | Papillary alveolar carcinoma | | |
| 181. Bretschneider (37) | 44 | | One child, 19 years ago, followed by postpartum ascending gonorrhea | Amber-colored discharge; cramplike pains in lower part of abdomen and sacral region | | Almost a month | Pan-hysterectomy | Left | Left tube had appearance of a hydrosalpinx; abdominal end densely adherent in pelvis and containing a papillary tumor | Papillary alveolar carcinoma | | |
| 182. Stancă (177) | 40 | | | Swelling of abdomen; obstipation and painful defecation; pains in lower part of abdomen; loss of weight | Cachexia; cystic tumor on right side extending almost to umbilicus | Two months | Double salpingo-oophorectomy; resection of omentum | Left | Left tube funnel-shaped, dilated at abdominal end and filled with encephaloid, papillary tumor; right ovary negative; metastases to left ovary and omentum; right hydrosalpinx | Papillary alveolar carcinoma | | |
| 183. Hillebrand (Amreich) (82, 7) | 48 | Single | Regular | Hard tumor in left lower part of abdomen, which gradually enlarged; no pains or discharge | Dense resistance, tumor the size of a fist, to left of uterus; many pea-sized to nut-sized nodules in pouch of Douglas | One year | Double salpingo-oophorectomy | Right | Ampulla of right tube as thick as a thumb and filled with dense, yellowish-white tumor; abdominal ostium closed; metastases to both ovaries, posterior surface of uterus and pelvic peritoneum; left tube negative; ascites | Papillary alveolar carcinoma containing cells resembling squamous epithelium | | |
| 184. Gullenhielm and Morlot (78) | 54 | | Three children (1 included for placenta praevia) and 5 miscarriages; profuse, prolonged and painful menses; menopause at 53 | Yellowish-white, fetid, discharge; pains in lumbar region and pelvis radiating to lower extremities | Mass, the size of a small mandarin, on the right side; the left adnexa palpable and tender | One year | Pan-hysterectomy | Right | Right tube distended, pyriform, and containing a tumor in its ampullary portion; ovary and uterus normal; left tube thickened and adherent | Papillary alveolar carcinoma | | |
| 185. Leuret and Leroux (109) | 32 | | Sterile; regular | History of salpingitis; leukorrheal discharge; pains in abdomen | | | | Right and left | Both tubes dilated and filled with papillary growth infiltrating wall; abdominal ostia open; almond-sized tumor in uterine canal; a few peritoneal metastases | Papillary alveolar carcinoma | | |
| 186. Goodrich (75) | 44 | | Three miscarriages; regular and scant up to 5 years ago; then infrequent | Subacute arthritis; occasional gush of thin fluid with a urinous odor and sometimes blood-tinged; pains in lower part of abdomen | Left adnexa tender and grew in size in a year | More than one year | Left salpingo-oophorectomy; right salpingectomy | Left | Left tube four times normal size and filled with spongiform, cauliflower, friable mass; right tube thickened; left ovary sclerotic | Diffuse epithelial growth | | |

TABLE 2.—Cases of Carcinoma of the Fallopian Tubes Reported in the Literature—Continued

| No. | Author | Age | Children: Menses | Symptoms | Physical | Dura- tion | Operation | Side | Macroscopic | Microscopic | Course |
|------|-----------------------|--------------------|--|---|---|---------------|-----------------------------------|----------------------|---|---|-------------------------------------|
| 187. | Küstner..... (102) | 42 Mar- ried | Sterile; regular | Curettage followed by sal- pingitis 2 years ago; pains in left lower part of abdo- men; slight yellowish dis- charge | Cystic tumor, the size of a hen's egg, to right of uterus and partly cystic tumor, the size of a fist, to left and behind uterus, almost filling pouch of Douglas | Two years | Double salpingo- oophorectomy | Right and left | Left tube S-shaped, dilated at ab- dominal end and containing a little serous fluid and a crumbly, medul- lary tumor partly free in the lumen; right tube of similar form and containing a greenish, jelly- like substance and numerous fine papillary growths arising from entire inner surface of tube; wall very thin; both abdominal ostia closed; ovaries normal | Papillary alveolar carcinoma | Well 6 months postoper- ative |
| 188. | Kalman... (80) | 40 | One abortion followed by adnexal in- flammation; regular; profuse | Serous discharge which later became like meat-water; marked loss of weight; continuous metrorrhagia, 1 month | The right adnexa thick- ened and tender; the left also thickened and indefinite | Two years | Panhyster- ectomy (vaginal) | Right and left | Right tube dilated into a sac at ab- dominal end which was filled by cauliflower tumor; left tube en- larged to size of a thumb and showing nodular and papillary growths in middle and ampullary portions; right ovary cystic; uterine fibroid | Papillary carcinoma | |
| 189. | Albrecht... (2) | .. | | Profuse, recently serosan- guineous, "hydrops tubae profusus" | | One year | | Right and left | | Primary car- cinoma | |
| 190. | Stübler..... (181) | 38 Mar- ried | Sterile; scanty; dysmenorrhea | Profuse discharge; recent acute attack of pain in abdomen; constipation; urinary difficulties | Tumor, the size of a child's head to right of uterus | | Double salpingo- oophorectomy | Right | Right tube composed of inner cystic one; the latter filled with caseous material and from its medial portion, papillary structure projecting; left tuberculous pyo- salpinx with appendix-like, serosal metastases; perioophoritis; metas- tases to omentum and serosa of uterus; enlarged lymph nodes along aorta | Papillary alveolar carcinoma; active tuberculosis; right ovary invaded by carcinoma at one point | |
| 191. | Schäfer..... (102) | 56 | | Fibroid uterus diagnosed 6 years ago and treated with roentgen ray and radium; return of metrorrhagia 18 months ago; continuous pains and feeling of pres- sure; constipation | Large tumor filling pelvis | Six years | Panhyster- ectomy | Right and left | Both tubes sausage-shaped, slightly tortuous and lumina filled with encephaloid tumors; uterine fibro- myoma, size of a man's head | Papillary alveolar carcinoma | Well 8 months postoper- ative |
| 192. | Ursprung... (180) | 53 | | Loss of weight; attack of pleurisy followed by inter- mittent vaginal discharge | Palpable mass in right lateral fornix; tender- ness in left fornix | One year | Panhyster- ectomy | Right | Right tube greatly dilated, adherent in pelvis, filled with blood and containing a broad-based papil- loma; left tube distended at tip and nodular in its mid-portion | | Well 1 year postoper- ative |

Microscopic Findings.—Sections (fig. 1) of the right tube revealed an overgrowth of fibrous tissue and infiltration of the wall with round cells. Projecting into the lumen were numerous papillary processes, composed of varying amounts of branching vascular connective tissue covered with a single layer of cylindrical epithelial cells. Cilia were not demonstrable. By partial fusion and infolding of the papillae, a complex picture was produced. In a few areas, the cells had broken through the basement membrane and deeply infiltrated the wall, forming solid strands of irregular polyhedral cells, small cysts lined with cuboidal epithelium and alveolar structures enclosing numerous glandlike spaces. The polyhedral cells were hyperchromatic and showed many mitotic figures.

The left tube showed a flattening out and fusion of the folds of the mucosa with the production of cystic spaces lined with one or two layers of cylindrical to cuboidal cells. At one point there was a large papillary outgrowth and infiltration

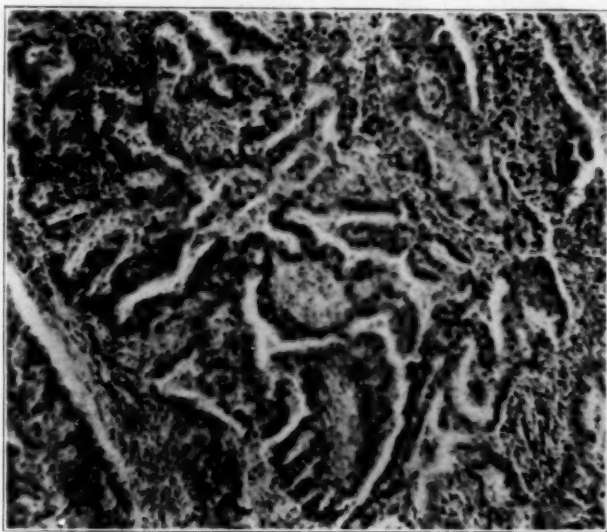


Fig. 1.—Papillary alveolar carcinoma of the fallopian tube; $\times 250$.

of the tubal wall similar in all respects to that found on the right side. The right ovary contained numerous metastatic foci composed of cuboidal to polyhedral cells having an alveolar structure.

The tumors removed from the abdominal wall and omentum had exactly the same characteristics as the tubal tumors.

Pathologic Diagnosis.—Bilateral papillary-alveolar carcinoma of the fallopian tubes; metastases to the right ovary and omentum; implantation metastases in the abdominal wound.

CASE 2.—History.—M. B., aged 52, a widow, was admitted to the hospital on Jan. 21, 1921, with the diagnosis of bilateral dermoid cysts.

Macroscopic Description.—The specimen consisted of a fallopian tube with an underlying cyst, a small tumor mass and an intraligamentous cystic tumor. The tube rested on and was intimately adherent to the cyst, its lumen ending blindly in the wall of the latter. Together they measured 8 by 6 by 5 cm. The tube was lined with thick, soft papillae, exhibiting many yellowish, necrotic areas. The

outer surface of the cyst was ragged and contained a few smaller secondary cysts, filled either with a clear fluid or thick, yellowish-white, mucoid material. Arising from the inner surface of the main cyst were numerous, small, papillary ingrowths.

The small tumor mass measured 3 by 1.5 by 1 cm., was firm in consistency, and on section was composed of dense grayish-white tissue containing areas of soft, yellow, necrotic material.

The large intraligamentous tumor mass measured 8 by 6 by 4 cm., was rounded and presented on its outer surface a few papillary excrescences. On section, a large cavity was found, filled with yellowish, mucoid and necrotic material. Numerous smaller cysts were also present containing a similar material and papillary ingrowths. The solid portion of this tumor was composed of dense grayish-white tissue.



Fig. 2.—Papillary-alveolar carcinoma of the fallopian tube; $\times 250$.

Microscopic Findings (figs. 2 and 3).—Sections of the large cyst underlying the tube showed a fibrous wall, which, in its outer portion, contained a considerable amount of smooth muscle not arranged in definite circular and longitudinal coats. Scattered throughout the wall were many caseous areas. They were often extensive, destroying large portions of the inner surface of the cyst. A few clearly defined tubercles were also seen, some of which contained giant cells. The intact portions of the cyst lining showed numerous branching papillary projections composed of a fibrous stem of varying thickness and covered with one to several layers of cylindrical epithelium. Cilia were not demonstrable. Buried deep in the cyst wall were numerous glandlike spaces lined with cylindrical epithelium, often raised as papillae into the lumina. The stroma was generally delicate, infiltrated with round cells, and in places resembled embryonic fat cells. Many calcareous particles were present. The cells lining the cysts, the glandular spaces and papillary processes were cylindrical, one to several rows in thickness, hyperchromatic, and many were swollen with mucoid material.

The tube showed the same type of tumor associated with tuberculosis. In places, the epithelial cells had penetrated the basement membrane and infiltrated the tubal wall in the form of narrow columns and small islands of cells.

The intraligamentous and small tumors showed a structure practically identical with that first described—extensive tuberculosis with caseation, papillary processes and infiltration of the stroma with the formation of solid alveoli and glandlike structures. A portion of the growth had undergone mucoid degeneration. The stroma showed a marked hyaline degeneration in some areas and edematous changes in others.

Pathologic Diagnosis.—Papillary cystadenocarcinoma of the fallopian tube associated with tuberculosis; secondary carcinoma and tuberculosis of the broad ligament.

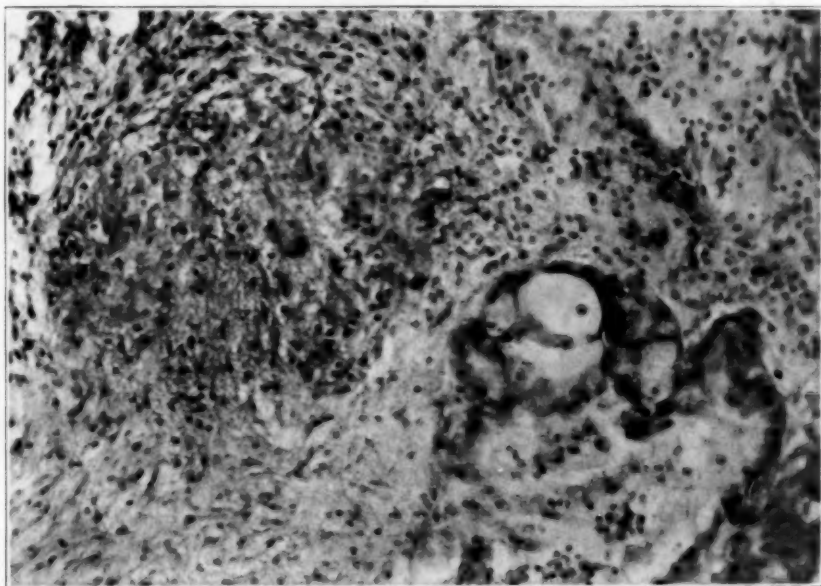


Fig. 3.—Tuberculosis in association with carcinoma; $\times 300$.

CASE 3.—History.—A. R., aged 43, married, was admitted to the hospital, Nov. 23, 1923, complaining of heaviness and fulness of the abdomen, pains in the back and vaginal discharge. She first noticed the fulness and heaviness in the lower part of the abdomen three months before admission, especially when putting on her clothes. A month ago, she began to have severe backache and for the past two years has had a profuse yellowish, vaginal discharge.

Her menses began at the age of 13, were regular, lasting two or three days, and not associated with pain. She had had a spontaneous, seven-month miscarriage twelve years ago, and a normal delivery ten years ago.

On physical examination, the uterus was markedly enlarged, extending to the umbilicus. The adnexa were not palpable.

Diagnosis.—Fibroma uteri.

Operation.—Supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed.

Macroscopic Description.—The left tube was roughly pear-shaped, the cystic dilatation at the fimbriated extremity measuring 15 by 10 by 7 cm. It was filled with a hemorrhagic fluid and numerous pedunculated and sessile papillary growths, arising from the tubal wall. The excrescences were yellowish, soft, and extended into the uterine portion, where they formed pinkish, cauliflower masses. The tubal wall was thin and trabeculated.

The adherent right ovary measured 2 cm. in diameter and presented on section a large hemorrhagic cyst and areas of edematous grayish tissue.

The right tube measured 7 cm. in length and had a circumference varying from 0.6 cm. at the uterine end to 2.7 cm. at the abdominal end. The serosa was injected and showed torn bands of adhesions. The mucosa was slightly roughened. The wall was 1 mm. in thickness and exhibited several small hemorrhagic areas.

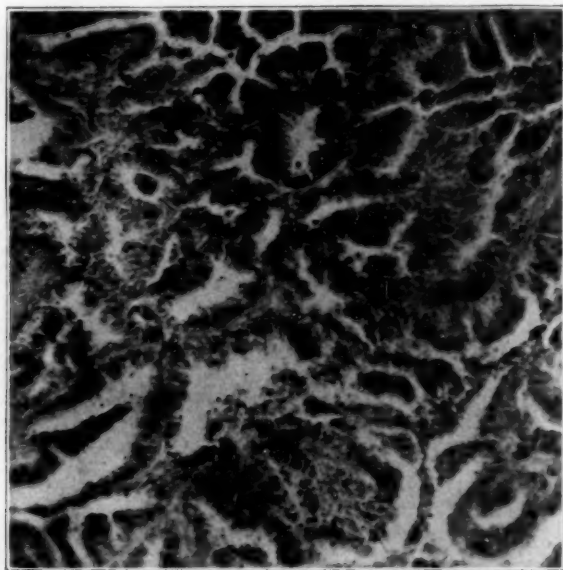


Fig. 4.—Papillary-alveolar carcinoma of the fallopian tube; $\times 250$.

The left ovary measured 4 by 1 cm. and presented on section a few simple follicular cysts, a large lutein cyst, and several small, hard, yellow nodules.

The uterus measured 8 cm. in length and 20 cm. in circumference around the fundus. Two nodules, the largest 2 cm. in diameter, and many small scattered, translucent, hard elevations were present on its peritoneal covering. The mucosa was thick and edematous.

Microscopic Description (fig. 4).—The lumen of the left tube was filled with papillary tumors composed of branching processes of vascular fibrous tissue covered with several to many rows of cylindrical epithelium. At their bases, due to being pressed together and by union of neighboring papillae, a pseudo-alveolar arrangement was produced—convoluted masses of polyhedral cells supported by a small amount of fibrous tissue exhibiting numerous small spaces and a few larger, glandlike lumina. The tumor elements extended deeply into the wall of the tube. Alveolar collections of polyhedral cells and many small lymphatic

deposits were present in the muscularis. There was a pronounced round cell infiltration of the entire wall, most marked in the muscular coat.

Both ovaries contained deposits of polyhedral cells in alveolar structures.

The right tube showed a complete obliteration of the mucous folds and a marked atrophy of the wall.

Sections of the uterus revealed a thickened endometrium. The glands were hyperplastic, convoluted and showed secretory activity. The stroma was edematous and infiltrated with many inflammatory cells. In areas, the stroma cells appeared enlarged. The myometrium was hypertrophic and contained small lymphatic metastases, a few of which were calcified. Metastases were also present in the serous coat. The two uterine tumors had the structure of a fibromyoma and an adenomyoma, respectively. Both contained tumor deposits, some of which in the adenomyoma were calcified.

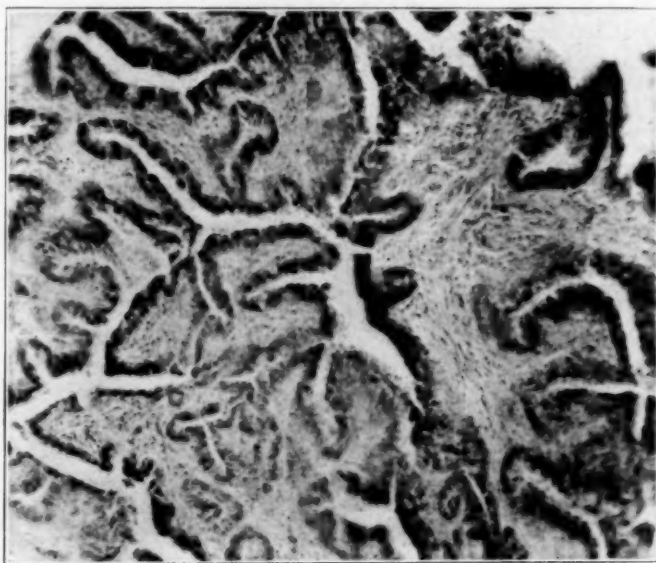


Fig. 5.—Papillary carcinoma of the tube; $\times 250$.

Diagnosis.—Carcinoma of the left fallopian tube; right hydrosalpinx; metastases to both ovaries and to the uterus; uterine fibromyoma and adenomyoma.

CASE 4.—History.—A. D., aged 39, married, was admitted to the hospital on Dec. 5, 1924, complaining of pains in the lower part of the abdomen. For five days prior to admission, she had had sharp, intermittent pains in the left side of the abdomen, radiating through the hip to the knee, which had become more or less general over the lower part of the abdomen. Vomiting was present at the onset. Eight years ago, she suffered a similar attack, associated with a white vaginal discharge, and since then has had occasional pains and headaches. Her menses were regular, profuse, lasting five days, and accompanied by slight pain and headache. She had been married for twenty-one years, and had had two normal deliveries, the last one nineteen years ago, and two induced abortions.

On pelvic examination, a tender, bulging mass, softened at one point, was made out in the posterior fornix. There was a slight vaginal discharge. Her temperature on admission was 103 F.

Treatment and Course.—A diagnosis of pelvic abscess was made, and under palliative treatment, her pains disappeared, the temperature dropped to 99 F., and the mass became smaller. She was discharged, Feb. 5, 1925.

Second Admission.—On March 9, 1925, she was readmitted complaining of occasional pains in the lower left quadrant, backache, dysmenorrhea, headaches and itching all over her body.

Examination at this time revealed an irregular, firm mass in the posterior fornix and an elastic, movable tumor, the size of a grapefruit, high up on the left side.

Operation and Course.—Bilateral salpingo-oophorectomy, appendectomy and ventral fixation were performed. The right tube burst during its removal, and a quantity of old pus escaped.

After several previous attacks, the patient died suddenly from an acute cardiac dilatation.

Macroscopic Observations.—Both tubes were markedly dilated and sacculated. The fimbriated ends were sealed. The mass composed of the right tube and ovary measured 5 by 4 by 2 cm., and the left 9 by 7 by 3 cm. The outer surfaces were rough, mottled with gray and red areas and showed a few adhesions. The mucosa of the left tube was hypertrophic, congested, and exhibited small, grayish areas of necrosis, while that of the right tube was smooth and congested. The walls varied from 2 mm. to 1 cm. in thickness. Both tubes were filled with pus.

The appendix showed a mild peri-appendicitis.

Microscopic Observations (fig. 5).—The left tube and ovary were converted into an abscess, the wall of which was formed partly by the tubal wall and partly by ovarian tissue. The abscess cavity was lined with granulation tissue, showing patches of necrosis and a marked infiltration with inflammatory cells. Practically the entire epithelium and a large portion of the musculature of the tube were destroyed. In one small area, in the inner half of the tube, a small epithelial growth was present. It was composed of irregular masses of tumor cells arranged in acini, cysts or enclosing lumina-like spaces. They were embedded in a dense, fibrous stroma infiltrated with round cells, and extended deeply into the muscularis. The tumor elements were cylindrical to cuboidal, hyperchromatic and showed increased mitotic figures.

The right tube showed a generalized increase in fibrous tissue and an irregular infiltration of the wall with round cells. The mucous folds were atrophic, flattened and partially fused. The outer layer of the wall, together with the inner portion of the ovary, formed the wall of a cyst. It was composed of hyaline fibrous tissue showing marked evidences of inflammation. There was no lining membrane.

Diagnosis.—Bilateral tubo-ovarian abscess with early adenocarcinoma of the left fallopian tube; chronic catarrhal peri-appendicitis.

SUMMARY

1. Carcinoma of the fallopian tubes is only a comparative rarity. This study is based on 192 cases gathered from the literature and four here reported.

2. This condition occurred between the ages of 40 and 55 in 66 per cent of the cases.

3. Sterility was present in 32 per cent.

4. The most common symptoms were pains in the lower part of the abdomen, a watery, often serosanguineous discharge and irregularities in the menses.

5. The tumor was situated in the right, the left or in both tubes in almost equal proportions.

6. The seat of the lesion was the middle, the outer third or both in the vast majority of cases.

7. Macroscopically, the tumor was either nodular or diffuse and histologically either papillary or papillary-alveolar in type.

8. Metastases, especially lymphatic, were common.

9. The association with tuberculosis was rare.

10. Evidences of inflammation either in the affected tube or that of the opposite side were present in a considerable proportion of the cases.

11. The operative results were extremely poor, due to the insidious onset of the disease, the difficulty in diagnosis and the few radical extirpations performed.

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STUDIES IN COCCIDIOIDAL GRANULOMA

II. MODE OF INFECTION *

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PHILADELPHIA

REVIEW OF LITERATURE UPON EXPERIMENTAL INVESTIGATIONS

In the first article of this series ¹ will be found a review of the clinical manifestations of coccidioidal granuloma with the report of a new case. In the present communication, I am presenting a review of the literature dealing with experimental investigations of the subject and a report of some of our own studies.

The organism causing this disease presents interesting phenomena because it possesses a double cycle. On artificial mediums, it presents a white, moldy growth, while in tissue it appears as spherical, double-contoured forms. H. C. Moffitt and May Ash accidentally discovered its growth on mediums, but for the knowledge of the cultural features and nature we are especially indebted to William Ophüls,² who in 1905 made careful cultural studies and identified the organism. It grows on all mediums, but especially well on 2 per cent glucose agar, 1 per cent acid, at 37 C. The filaments or aerial hyphae are not very long, and they seem to penetrate the medium so that the growth becomes adherent. Old cultures look white like dry snow, or have a cottony appearance. In a hanging drop preparation one sees septate, branched mycelia or hyphae, which form an intricate meshwork.

Wernicke³ and Gilchrist⁴ gave the first descriptions of its form in tissue. Gilchrist's description cannot be improved on:

The parasite, when fully grown, is enveloped in a distinct double-contoured capsule, and then appears as an almost perfectly spherical organism. . . . These forms vary from 15-27 microns in diameter and consist of a thick, well defined, spherical capsule, which can be deeply stained. Between the capsule and the contents is a clear refractive layer which usually does not stain or is stained with difficulty. This clear zone appears homogeneous and structureless; it varies in thickness from 2-3 microns, but is hardly discernible when the organism is undergoing sporulation. The protoplasm surrounded by the clear layer stains very readily: it is for the most part finely granular but contains also not a few scattered coarse granules, sometimes arranged around the

* Aided by the Sabin W. Colton, 4th, Memorial Research Fund at the William Pepper Laboratory of Clinical Medicine, University of Pennsylvania.

1. To be published.

2. Ophüls, William: J. Exper. Med. **6**:443, 1905.

3. Wernicke: Centralbl. f. Bacteriol. u. Parasit, 1892.

4. Rixford, Emmett, and Gilchrist, T. C.: Johns Hopkins Hosp. Rep. **1**: 209, 1896.

periphery, at other times entering into the formation of a net-work. . . . The "protozoa" present in this case are reproduced by sporulation. . . . The number of sporozoites which are finally developed from one organism varies, but is usually very large. During the process of sporulation the capsule can be observed to become thinner and thinner until it consists only of a faint but well defined membrane which finally bursts. Just before this bursting stage, the organism changes its shape and assumes an oval form. The rupture takes place at one side or at both sides of the ovoid. One photomicrograph, fig. 17, shows a number of very fine prickles extending out from the capsule, especially at the sides.

We have found these "prickles" (fig. 1) in several sections, and they are found only in the adult organisms, when they are ready to liberate the young forms. We are able to confirm this method of sporulation, but think that the sporulating stage assumes an elliptical rather than an oval form (fig. 2).

Various attempts have been made to study the growth from mycelium to the double-contoured form and vice-versa. In 1905, Ophüls suspended some pus that he obtained from an abscess near a testicle in beef tea hanging drops, and observed three protozoon-like forms. In twenty-four hours, mycelium had developed from two of the three organisms. He repeated this process several times. Ophüls maintains that the spores are typical chlamydospores and not oidia.

Wolbach⁵ attempted to connect the two phases. He found that on an agar hanging block preparation he could produce mycelium—"8-10 filaments may be seen to grow from a single sphere, apparently from the capsule." To demonstrate the change from filaments to spheres, he used two methods. One was to make intravenous injections into rabbits and to study the histology of the lungs at different stages (from twenty-four hours to several weeks); and the second method was to introduce into the peritoneal cavity of rabbits a pure culture sealed in collodion capsules and to examine these animals at periods varying from a few days to weeks. He says: "Both methods have yielded the same results, and have shown that each sphere develops from a segment of the mycelium." In the study of the lungs, he explains:

The masses of filaments act as small emboli which are very soon invaded by leucocytes and endothelial cells, so that at the end of forty-eight hours there are large areas of inflammatory reaction in which it is very difficult to find the organisms.

After inoculation most of the filaments disappear with great rapidity; at the end of twenty-four hours they are broken up into coarse granules which stain with eosin and it is only at the center of the embolus that we find these preserving the form of the filament.

Forty-eight hour lesions show rows of such segments with increased size, while the membrane has undergone a change which makes it take an intense stain with eosin. At this time we also get the beginning of a hitherto

5. Wolbach, S. B.: J. M. Res. **13**:53, 1904.



Fig. 1.—Spiculated form in area of granulation tissue.

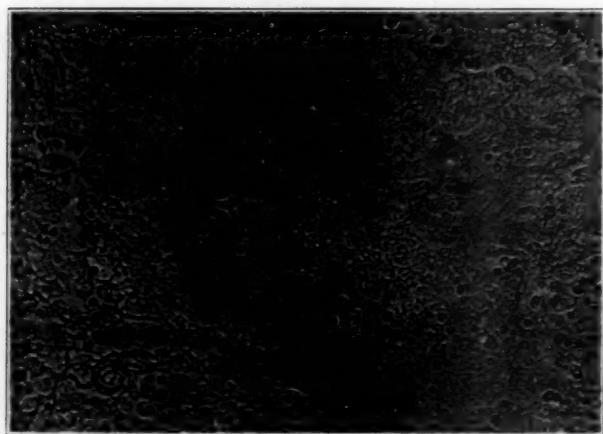


Fig. 2.—Bursting of the capsule.

unobserved phenomenon, the production of clubbed and pointed projections radiating from the membrane, first, of what is the mycelium and of what later becomes the spherical bodies (fig. 14). These segments continue to increase in size so that at the end of seven days we get perfect spheres, some of which may have formed spores.

Employing collodion capsules he obtained similar results, namely, "the swelling of the individual segments and the acquisition of a thick capsule. The spheres thus formed increase in size as in tissue, and finally complete the cycle by endogenous sporulation."

MacNeal and Taylor⁶ report that concerning a hanging drop preparation:

Many of the spheres, however, underwent a remarkable development. The capsule was penetrated at several points by blunt protoplasmic outgrowths from the interior protoplasm. The rapidity of development of these shoots in some instances was such as to give the impression of ameboid movement at the growing tips. The shoots, at first naked cylinders of granular protoplasm, soon produced a definite, more hyaline wall about them branched abundantly and irregularly and developed septa. After several hours ovoid bodies of more homogeneous structure were numerous, within many of the cells. After twenty-four hours, the circular colony had attained a diameter of one millimeter and was made up of branched interlacing septate threads from two to eight microns in diameter, with the old capsule of the original sphere at the center.

He supports the findings of Wolbach. From our observations, we think that these spheres are probably oidia.

The classification of this organism is still an open question. Unfortunately, there has been great confusion in the literature. However, it is now recognized that the organism which causes coccidioidal granuloma is distinctly different from the organism which causes blastomycosis.

At the present time it seems that the organism of coccidioidal granuloma reproduces by internal sporulation while blastomyces reproduces by budding. Stoddard and Cutler,⁷ have separated the diseases neatly in the following manner.

Coccidioides immitis is definitely an ascomycete on account of its endosporulation, and is seen to be in close biological relation to the yeasts.

True yeast infection, produced by an organism which reproduces by budding. It produces no true mycelium, forms endospores under certain conditions, and usually ferments sugar. The organism is rather feebly pathogenic for animals. There are two authentic cases in man, the first being Busse's. . . . The organism has an adventitious capsule occasionally in human and animal lesions, but does not produce a gelatinous matrix and does not have even a capsule in brain lesions in animals.

6. MacNeal, W. J., and Taylor, R. M.: J. M. Res. **30**:261, 1914.

7. Stoddard, J., and Cutler, Elliott: Monograph of Rockefeller Inst. for M. Res., No. VI, January, 1916.

Torula infection, produced by a yeast-like organism, distinguished from yeasts by the absence of endospore production under all circumstances. It never produces mycelium, usually does not ferment sugar, and reproduces by budding alone. . . . Six cases are known in human beings. In localization the nervous system especially is affected, to a less extent other organs, never the skin as part of the general infection. . . . The organism produces peculiar intracerebral lesions, consisting of a lysis of the cerebral tissue, with only a very chronic proliferative reaction which is often almost lacking, and fills the lesion with a peculiar gelatinous material holding the organisms separate, in which occasionally threads and star-like processes form. In other organs it produces, as a rule, nodular lesions resembling miliary tubercles, which finally become dense connective tissue masses.

Oidiomycosis is caused by an organism reproducing by budding in tissue, and forming mycelium in cultures. There is no endospore production. There are over thirty recorded cases of systemic involvement, and more numerous cutaneous cases. In localization oidiomycosis affects especially the skin and subcutaneous tissues, no reported systemic cases being free from such involvement; it often involves bones; it affects all internal organs including the brain, but has not yet produced lesions in the brain which have caused symptoms until just before death from the general infection.

MacNeal and Taylor gave Brumpt's classification:

Stem Fungi (exclusive of bacteria):

Class I: Phycomycetes (vegetating hyphae are not septate or at any rate not until they are old).

Class II: Ascomycetes (mycelium is septate. Spore sacs, asci, are produced, containing eight to thirty-two or more spores; other methods of spore formation variable).

Class III: Hyphomycetes (shoots reproducing by conidia only, so far as is known).

Brumpt places the organism of coccidioidal granuloma in the class of hyphomycetes while MacNeal places it in the class of ascomycetes. As yet there is no unanimity of opinion as to its classification.

The organism is pathogenic for animals. Gilchrist was not successful in his inoculation experiments. He rubbed bits of tissue that contained the organism and that had been reduced to pulp, into the scarified surface on the leg of a dog and the same on the inner side of the dog's ear. Sores developed at these places.

Those on the ears, however, healed spontaneously at the end of a few weeks but that on the leg gradually spread till at the end of a month it was three quarters of an inch wide and one and one half inches long. It had the form of an ulcer with slightly elevated margins, consisting of swollen papillae and resembled somewhat the lesions on the patient's face. The inguinal glands enlarged till a mass as large as a man's fist was formed. The sore was excised. The incision healed rapidly. The glandular swelling, however, continued to increase; fluctuation appeared and the abscesses opened spontaneously. The whole mass of femoral and inguinal glands was excised. . . . The glands were found to be matted together by inflammatory tissue, and were so adherent to the surrounding structures that more or less of the

abdominal muscle had to be removed with them. The wound healed kindly. The dog recovered and seemed none the worse for the experiment.

Pus from the ulcer of the leg showed protozoa at various times, and pus from the glandular abscesses showed the organism. "Sections from the lesions showed marked pathological changes which as far as the corium was concerned, were similar to those produced in patient."

Ophüls reports: "The fungus is pathogenic for dogs, rabbits and guinea-pigs, probably other animals also, and in them produces lesions very similar to those which we encounter in human beings in this disease." Many of the infected guinea-pigs developed a periorchitis from which the organism was isolated. Therefore, suppurative periorchitis in guinea-pigs is not pathognomonic for glanders. In the guinea-pigs that Ophüls inoculated intraperitoneally, he found small nodules and abscesses in the testicles, omentum, spleen, kidneys, liver, lung and pancreas. Protozoon-like bodies were found in fresh specimens from the nodules and the abscesses. A rabbit which received 0.5 cc. of a suspension of a culture grown on beef tea injected into a large vein of the ear died in four weeks and showed many miliary nodules in the lungs, kidneys and spleen. Fresh teased specimens showed protozoon-like bodies in all the nodules. Experiments on frogs were not successful. Several have been successful in inoculating rabbits and guinea-pigs subcutaneously, intraperitoneally, intravenously and subdurally.

Some serologic experiments have been attempted. Cooke⁸ found that there were no specific complement fixing bodies or agglutinins. No specific skin reaction was demonstrated. "Precipitins, however, could be demonstrated." He was unable to produce a diffusible toxin. "A diffusible toxin could not be demonstrated, as shown by the survival of guinea-pigs (250 grams) inoculated subcutaneously and intramuscularly with a quantity of broth filtrate varying from 0.5 to 2 cc."

Stoddard and Cutler were unable to demonstrate an agglutination test of diagnostic value.

Bump⁹ reports some observations on the growth of *coccidioides immitis*. He studied the p_H and observes "it grows well in mediums with a p_H variation of from 2.02 to 12.13, and therefore can easily withstand the extremes of p_H change in the soil."

EXPERIMENTS ON MODE OF INFECTION

The first step in our investigation of this disease was to determine the probable modes of infection, the purpose being to discover if possible the most important mode for man. It was, of course, hoped that we

8. Cooke, J. V.: Arch. Int. Med. **15**:479, 1915.

9. Bump, Warner S.: J. Infect Dis. **36**:561, 1925.

would be able to produce the disease in exactly the same form as seen in human beings, by some definite methods of infection. So far, the results have not been perfectly satisfactory in this direction, although we have been able to make injections into animals in certain ways which can be repeated at any time. The material used was our culture CAR that we have already described in a previous article. It is grown on 2 per cent glucose agar, p_H 7.

Three sets of rabbits and of guinea-pigs were employed in the following ways at three different times:

1. One platinum loopful of the dry mold was rubbed over an abraded surface of the skin on the back of the head.
2. One platinum loopful of the dry mold was rubbed over the mucous membrane of the nose.
3. One platinum loopful of the dry mold was rubbed over the mucous membrane of the mouth.
4. One loopful of the dry mold was suspended in salt solution and was injected into the trachea through the skin of the neck.

(1) In the first set of rabbits in which the culture was smeared over the skin, two of the rabbits died, one in two weeks and the other in four months, and the third is alive and thriving. At necropsy, the dead animals showed enlarged testicles and miliary nodules throughout the lungs. The other organs were apparently negative. Microscopically, at the point of inoculation in the skin, granulation tissue was found in which were sporulating forms. The lungs showed small areas of peribronchial inflammation, but no organisms were found—not even in the nodules.

The guinea-pigs of this set died within from three to four weeks, having lost about 50 per cent in weight. The weight drop was so striking that we thought it important enough to make it the subject of an extra paragraph.

The guinea-pigs that had received injections would maintain their weight and in some instances gain a few grams during the first ten to twelve days. Then in one or two days there would be a decided drop, for instance, from 560 Gm. to 390 Gm. in a period of three days. The change was perceptible from one day to the next. After the tenth or twelfth day they would not eat, were very inactive and would fall over easily. Guinea-pigs from 400 to 500 Gm. maintained their weight longer than those of from 300 to 400 Gm.

At necropsy, in one guinea-pig, minute nodules were seen in the liver and in the lungs. Another guinea-pig showed nodules in the liver only. The third guinea-pig showed enlarged and hemorrhagic cervical and mesenteric glands. In all three guinea-pigs the testicles were moderately enlarged and injected. In one, the left testicle was covered with pus in which the organism was found. Microscopically,

the lungs showed a slight edema and some hemorrhage. There was some inflammation in a few peribronchial areas in which the organisms were found. The heart was negative. The liver showed some cloudy swelling and small areas of cellular infiltrates, in which the organism was not found. The spleen showed diffuse follicular hyperplasia. The kidney showed a moderate amount of edema.

(2) In the second set in which the culture was smeared over the mucous membrane of the nose, one of the rabbits was chloroformed after six weeks and the remaining two are still alive and doing well. At necropsy, in the chloroformed animal, no nodules were found, but the testicles were enlarged. Microscopically, the characteristic organism was found in the lungs in tiny cellular infiltrates.

The three guinea-pigs died within from two to four weeks, having lost about 50 per cent in weight. They showed the characteristic weight drop. At necropsy, minute nodules were found in the lungs and liver. The microscopic picture was like that above, and the organism was found in the lungs in one case.

(3) In the third set, in which the cultures were smeared over the mucous membrane of the mouth, the rabbits were resistant. One rabbit was chloroformed at the end of six weeks and the remaining two are alive and doing well. The chloroformed rabbit, at necropsy, showed a few nodules in the liver and enlarged testicles. No organisms were found microscopically.

The guinea-pigs in this set died within three or four weeks and lost about 40 per cent in weight. They showed the characteristic weight drop. At necropsy, a few nodules were found in the liver of one guinea-pig. In another pig, the cervical and mesenteric lymph nodes were enlarged and hemorrhagic. Microscopically, the organism was found in the liver. Culture from the cervical gland was characteristic.

(4) In the fourth set in which the culture was suspended in salt solution and injected into the trachea, through the skin, one of the rabbits was chloroformed after six weeks, and the remaining two were apparently well. In the chloroformed animal, pin point nodules were seen in the lungs. The other organs were negative. Sporulating forms were found in the lung.

The guinea-pigs in the fourth set died within three or four weeks and lost about 50 per cent in weight. In one, minute nodules were found in the lungs. In another, the lymph glands were injected, and there was a periorchitis. Microscopically, the organism was found in the lung and the spleen.

As the laboratory animals were thus infected by using the dry culture CAR through the skin, the trachea and the mucous membrane of the mouth, we thought it worth while to investigate further. In order

to approach the natural ways of infection as closely as possible, we attempted breathing and feeding experiments. A galvanized box was made so that it could be autoclaved. An anatomizer which contained glucose broth culture of CAR was inserted at one end of the box and cotton plugged a small opening at the other end. The guinea-pig was placed in the box and the culture was sprayed into the box. Thus the animal was exposed to contaminated air. However, we were aware that this does not insure the value of aspiration in an experiment, since the organisms might fall on the pharyngeal mucosa and be swallowed. It could only demonstrate that if infection occurred, air dissemination is possible. Primary inspiratory infection has already been demonstrated by the intratracheal insufflation.

In the feeding experiments, this same galvanized box was used. Some lettuce which had the CAR culture smeared over it was put in the box in which a hungry guinea-pig had been placed. If the guinea-pig refused to eat the lettuce, it was tried again until he did. These two experiments were repeated at three different times with several guinea-pigs each time.

In the first series, four guinea-pigs were fed lettuce that was contaminated with CAR culture and died within eighteen to twenty-five days, having lost on the average 40 per cent weight without gross lesions. The three guinea-pigs that were exposed to contaminated air died in twenty-four and twenty-five days, having lost 50 per cent weight. At necropsy, the omentum and all the organs were moist. No nodules were seen. The cervical and mesenteric lymph nodes were enlarged and injected. Microscopically, they showed nothing of particular note. The lungs showed edema and some hemorrhage. The liver showed some cloudy swelling. No organism could be seen. However, we obtained a culture from one of the mesenteric glands.

In the second series, a guinea-pig that ate contaminated lettuce died in twenty-eight days, having lost 45 per cent in weight without gross lesions. The four guinea-pigs that were exposed to contaminated air died in twenty days, having lost on the average 50 per cent in weight. We obtained the same picture as described above.

In the third series, the three guinea-pigs that fed on contaminated lettuce died in thirteen days, having lost 37 per cent in weight without gross lesions. The three guinea-pigs that were exposed to contaminated air died in eleven days, having lost 45 per cent in weight. The necropsies were striking in their negativeness. All the organs appeared moist. There were a few hemorrhagic areas in the lungs. No miliary nodules were seen in any of the organs. The lymph nodes appeared slightly injected. No gross lesions could be seen in the stomach or intestines. The testicles were not enlarged.

Microscopically, in two of the guinea-pigs that were exposed to contaminated air the organism was seen in the cervical glands. In one of the guinea-pigs that ate contaminated lettuce, the organism and empty shells were seen in the walls of the intestine. Also, in another pig that ate contaminated lettuce, the organism was seen in the lymphatic tissue of the postpharyngeal wall and in the mesenteric gland. Culture was recovered from a cervical gland. It is difficult to identify the young forms histologically, and there are probably young forms in some of these tissues, but we are not able to demonstrate them under the microscope. We feel that the loss of weight and death of the experimental animals were due to dissemination of the infection, although the demonstration of the organisms was unsuccessful. The forms definitely identified have been the adult or sporulating stages. We believe that the spreading of the small spores, which are so difficult to find and identify in tissue, is of prime importance in the dissemination of the disease within the body. This thought is based on the following facts: Many animals die without gross lesions, and, within the microscopically discovered infiltrations, no adult forms are to be found. Yet from such animals it is possible to recover cultures. The minute lesions and the cultures in all probability come from the stage of metamorphosis for which we have at present no certain identification. It is with this part of the pathogenesis that we are now occupied.

SUMMARY

Experiments dealing with the mode of infection were attempted by rubbing one platinum loopful of the dry mold over an abraded area of the skin, over the mucous membrane of the nose, over the mucous membrane of the mouth and by suspending a platinum loopful in salt solution and injecting it into the trachea through the skin. Also, experiments dealing with the natural mode of infection were attempted by feeding guinea-pigs with lettuce contaminated with culture and exposing guinea-pigs to air contaminated with broth culture.

Rabbits were more resistant than guinea-pigs. All the guinea-pigs died spontaneously in from three to four weeks. They maintained their health until the tenth day and then lost in weight quickly. There was a characteristic drop in weight. At necropsy, some of the pigs showed minute nodules in the lungs and liver, some enlarged mesenteric and cervical lymph nodes, some suppurative periorchitis. Microscopically, there were small areas of peribronchial inflammation, edema and hemorrhage in the lung. The liver showed some cloudy swelling; the spleen follicular hyperplasia; the stomach and intestines were normal; the kidney showed a mild acute interstitial nephritis; the lymph glands some hemorrhage, and the brain showed edema. The organism was found in the lung, liver, intestine, lymph gland and spleen.

Guinea-pigs fed coccidioides culture on lettuce showed no gross and insignificant microscopic lesions; few adult forms and shells in the intestines and some adult forms in the pharyngeal lymphatics; they lived longer than pigs that breathed culture. The animals that breathed the culture showed deep congestion or hemorrhages in the lungs, and fluid in the pleura; but no more of the adult forms could be found in the lungs than were discoverable in the tissues of the feeding pigs. These differences suggest greater potency of infection by breathing contaminated air than by eating infected lettuce.

As the animals were infected by using the dry mold through the skin, the trachea and the mucous membrane of the mouth, and by exposing the animals to contaminated food and air, it is probable that coccidioidal granuloma may be transmitted through the skin, as well as the respiratory and gastro-intestinal tracts.

Laboratory and Technical Notes

AN ANALYSIS OF THE BOTELHO SERUM TEST FOR CANCER *

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AND

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The value of the treatment of cancer in its early stages emphasizes the desirability of laboratory aid in the diagnosis of incipient lesions. Many tests to determine the presence or absence of cancer in man have been advocated, but none has proved of value. One of the most recent ones, which depends on obtaining a precipitate in serum under certain conditions, has been used by Botelho. Early reports suggested that this test might be valuable, and the study presented here was undertaken in an attempt to determine its clinical importance as an aid to diagnosis.

LITERATURE

A number of publications by French and Italian physicians on Botelho's so-called serodiagnostic test have appeared recently. Several of these reports have been published since the present study was begun. Wilbouchevitch¹ first described the technic of performing the reaction, and gives in his paper the results he obtained by its application to the serums of a group of patients. Papers concerning the results of its use have been published also by Cabanis and Foulquier,² P. and M. Guerin,³ Sabrazes and Muratet,⁴ Palmieri,⁵ Blouquier and Brugairolle,⁶ Peracchia,⁷ Giauni,⁸ Malaguti,⁹ and Fichera.¹⁰ Malaguti obtained a positive reaction in but 56.25 per cent of serums from patients with

* From the Medical Service of the Collis P. Huntington Memorial Hospital of Harvard University.

1. Wilbouchevitch, A.: *Mém. Soc. de biol.* **87**:1339, 1922.
2. Cabanis, A., and Foulquier, C.: *Mém. Soc. de biol.* **88**:1011, 1923.
3. Guerin, P., and M.: *Mém. Soc. de biol.* **88**:1251, 1923.
4. Sabrazes, J., and Muratet, L.: *Arch. d. mal. du coeur* **16**:841 (Dec.) 1923.
5. Palmieri, V. M.: *Rassegna Internaz. Clin. e Ter.* **5**:330, 1924.
6. Bloquier and Brugairolle, A.: *Gaz. d. hôp.* **45**:745, 1924.
7. Peracchia, G. C.: *Tumori* **11**:318 (Feb.) 1925.
8. Giauni, G.: *Riforma med.* **41**:219, 1925.
9. Malaguti, A.: *Riforma med.* **41**:538 (June) 1925.
10. Fichera, G.: *Compt. rend. Soc. de biol.* **93**:1116 (Nov.) 1925; *Rev. de la Soc. argent. de biol., Buenos Aires* **1**:335 (Sept.) 1925.

cancer, while the others found the reaction positive in 75 per cent or more of their cases. It would appear that the majority of the patients with cancer studied by the different authors were in a relatively advanced stage of the disease. Peracchia⁷ reported that with clinical improvement following surgical removal of neoplasms, or roentgen-ray or radium irradiation, the test often became negative, while Wilbouchévitch¹ did not note such a change soon after irradiation treatment. All the different authors obtained positive tests on the serums of patients who were distinctly sick with various forms of infections and other conditions known to cause an abnormal "colloidal state" of the blood, as cirrhosis of the liver, uremia and pregnancy. The percentage of positive tests on the serums of persons suffering from various noncancerous conditions varied from 7 to 60 per cent in the series of the different authors. Rather few reports are given as to the results obtained on testing the serums of normal persons, but it appears that less than 3 per cent have yielded a positive reaction. Although no one has concluded that the Botelho reaction is specific for cancer, several have suggested that it is of diagnostic value because of the relatively high percentage of positive tests obtained on the serums from patients with cancer.

Such reports as that of Peracchia,⁷ who obtained positive reactions on about 80 per cent of 172 serums from cancer patients and on but 10 per cent of 103 serums from persons not having this disease, suggest that the test is valuable. The experimental work of Itchikawa and Baum¹¹ suggests the same. These workers reported that the Botelho reaction was negative on the serums of normal rabbits but became positive on the serums of all rabbits in whom tar cancer was induced. Such observations as these are misleading, as the controls were not in a state of general health comparable to those with cancer.

METHODS

The Botelho reaction is based on the fact that a precipitate is formed when a potassium iodide-iodine solution is added to blood serum in the presence of a dilute solution of nitric acid. Different serums, in constant amounts, require varying amounts of the iodine solution to produce a permanent precipitate. If, under conditions given below, the precipitate persists when 1.3 cc. or less of iodine solution is added, the reaction is considered positive, but is negative if more is required.

The solutions are prepared from commercial chemically pure materials as follows:

1. Nitric Acid Solution: One cubic centimeter of 36 degree Baumé nitric acid (specific gravity 1.3325 at 15 C.) is added to 100 cc. of 0.75 per cent sodium chloride solution.

2. Potassium Iodide-Iodine Solution: Two grams of potassium iodide and 1 Gm. of iodine are dissolved in 210 cc. of distilled water. In order to dissolve

11. Itchikawa, K., and Baum, S. M.: *Bull. de L'Ass. franç. p. l'étude du cancer*, January, 1924.

the iodine completely, the first 20 to 30 cc. of water must be added drop by drop, and then 10 cc. at a time. During the process, the solution must be stirred constantly. This solution is unstable but will keep for at least two weeks when stored in a brown glass bottle having a ground glass stopper.

Exposure to air or light produces some change in the solution which may lead to false "negative" results.

The test is performed on serums obtained from 5 to 10 cc. of venous blood withdrawn from individuals who have fasted for twelve hours. The blood is allowed to clot at room temperature and, if necessary, is corrected to a protein content of 7.8 to 8.0 Gm. per hundred cubic centimeters. An Abbé refractometer may be used and the percentage of protein calculated by the method of Reiss. If the serum is too dilute, it is allowed to evaporate in an incubator; if too concentrated, it is diluted with 0.85 per cent sodium chloride solution.

Different workers have performed the test with slightly varying technics. For some months the results of our tests appeared in such discord with those reported by others that it seemed that we were not performing the test properly. Then, through the kindness of Dr. Chester M. Jones, we received direct from Dr. Botelho (on Dr. Hartman's service at the Hotel Dieu, Paris) a detailed description of the method of procedure most recently (October, 1925) advocated by him. The tests reported on below include only those made by this technic, which, in addition to the details given above, is as follows:

1. The serum is removed from the icebox, if it has been stored, and allowed to attain room temperature.

2. Three cubic centimeters of the nitric acid solution is placed in a test tube 10 cm. in length with a bore of about 1.5 cm.

3. To this is added 0.5 cc. of the serum (corrected to 7.8 to 8 Gm. protein per one hundred cubic centimeters). This is shaken until the serum and nitric acid solution are thoroughly mixed.

4. Then 0.5 cc. of the iodine solution is added. A flocculent precipitate forms at the junction of the iodine solution and the nitric acid-serum mixture. The tube is shaken very gently at first, and then gradually more violently until the precipitate has been completely dissolved.

5. Five-tenths cubic centimeter of the iodine solution is added and shaken as before.

6. To this 0.3 cc. of the iodine solution is added and shaken gently until the precipitate is dispersed throughout the tube. The procedure is then completed. If the contents of the tube remain perfectly clear, the reaction is negative. If there is definite cloudiness after 1.3 cc. of the iodine solution have been added, the reaction is considered positive. Observations are best made in artificial light, using a 25 watt electric light bulb as a background. If the reaction is negative, the degree of negativity should be determined by the further addition of iodine solution, 0.2 cc. at a time, until a permanent precipitate appears.

MATERIALS

The Botelho reaction, has been applied to the serums of 145 individuals.¹² This group consisted of seventy-nine patients with cancer,

12. Some of the samples of blood were obtained from patients at the Peter Bent Brigham Hospital, the Boston City Hospital, and the Massachusetts General Hospital.

sixty-two suffering from other disease conditions and four normal persons. The latter were tested numerous times. The diagnosis of cancer was made by microscopic examination of excised tissue in 65.8 per cent of the cancer cases.

The only recognized lesion in thirty-five of the patients with cancer was a relatively superficial tumor about the face, mouth, throat or external genitalia, with regional lymph node enlargement in some. The other cases of cancer included fourteen of the breast, twelve of the cervix of the uterus and ten of the gastro-intestinal tract. All the patients in the first group appeared to be in at least a fair state of physical health, and the majority had the appearance of being well. Some of those in the second group seemed in fair health, but about one-third were distinctly sick.

The state of health of the majority of the patients comprising the control group was in striking contrast to the majority with cancer. The former were obviously sick and quite unable to be out of bed. These patients had such diseases as chronic nephritis, cirrhosis of the liver, pneumonia, pulmonary tuberculosis, typhoid fever, peptic ulcer, lead poisoning, diabetes mellitus, pernicious anemia, various types of lymphoblastoma and chronic myelogenous leukemia.

RESULTS

The serums of 31 (39.3 per cent) of the patients with cancer gave positive reactions, as did 38 (61.3 per cent) of the serums from the other patients. None of the serums from normal persons yielded positive tests. Patients with lymphoblastoma, leukemia and pernicious anemia, conditions considered by some to be in the nature of a malignant neoplasm, were included in the control group. However, there was no greater percentage of positive tests on the serums of these patients than on those of patients suffering from infections, nephritis and cirrhosis of the liver. The test was more often positive on the serums of distinctly sick persons with cancer than on the serums from those in whom the disease had caused no obvious impairment of general health. Likewise, in the control group of patients, the serums of those not particularly ill usually gave negative tests, as did those of normal persons, while the serums from distinctly sick people usually gave positive reactions.

Experiments were performed to determine the effect on the reaction of various modifications of the technic. Marked changes in the results were obtained when the amount of the serum used or the protein concentration of a serum was varied. If the amount of the serum was increased, larger quantities of the iodine solution were necessary to produce a permanent precipitate. The same was true when a serum was concentrated so that its protein content was high. If more than 0.5 cc.

of serum was used or if the protein concentration was above 8 Gm. per hundred cubic centimeters, false "negative" results frequently were obtained.

Some of the serums tested the same day the blood was taken required more and others less of the iodine solution to cause precipitation than when tested after standing twenty-four hours. No constant variation in the degree of positivity or negativity of a serum was noted when it was tested repeatedly after remaining in the icebox a day, or from two to twenty days. Serum tested immediately after being removed from the icebox, or while cold, required slightly greater amounts of the iodine solution to cause cloudiness than the same serum at room temperature. Cloudiness appeared more readily after serum had been heated in a water bath at 55 C. or placed in an incubator at 37.5 C. for one-half hour than when at room temperature. Serum tested after remaining in contact with the blood clot for from six to ten hours behaved in no appreciable way differently than serum soon removed from the clot; nor did the presence of a very slight amount of hemoglobin in the serum definitely alter the test.

COMMENT

It is evident that Botelho's test is not specific for cancer, and it would appear that the number of positive reactions in any group of persons depends in a large measure on the general state of health. If one tests the serums of sick persons with cancer, a high percentage of positive reactions are to be expected. A comparison of such a series of tests with those made on the serums of normal persons or those not particularly sick would make this test appear offhand as of diagnostic value. On the contrary, contrast the results of Botelho's test on serums from a group of patients with incipient and superficial cancer with those from a group of noncancerous but distinctly sick patients. Rather few of the former group will give a positive reaction and many of the latter group will do so. This demonstrates clearly the inadequacy of the test as a diagnostic one.

It is well known that alterations in the "colloidal state" of the blood occur in many conditions, especially in persons who are ill with infections, toxemias and cancer, and in pregnant women. Such a change is demonstrable in numerous ways, as by an abnormal rate of sedimentation of red blood cells, by a delayed reaction of the oxidation of methylene blue in serum, by alterations in the absolute and relative amounts of the globulin in proportion to the albumin of the blood, etc. Such determinations have been advocated, by a variety of technics, as tests for cancer, and also to obtain prognostic information in many diseases, for as a sick person improves the "colloidal state" of the blood returns toward

normal. None of these tests, several of which have recently been reviewed by Fry,¹³ has proved of value in diagnosis. All appear to be related in some way to the globulin-albumin ratio of the blood and may be looked on in the nature of flocculation reactions. Botelho's reaction seems to be of this nature and but another test to be added to those that are not dependent on specific antibodies, but merely on the physical state of the blood colloids. Kennaway,¹⁴ among others, has shown that serums from patients with cancer and other diseases may show, especially when cachexia has been present, an absolute or relative increase of globulin in proportion to albumin. It is probable that a positive Botelho reaction depends on such an abnormality, and the work of Fichera¹⁰ bears out this view. He obtained positive tests on the serum of normal guinea-pigs, which is rich in globulin, and negative tests on the serum of normal rabbits, in which albumin predominates. He also noted that in human serums giving positive tests there was "an increase of sero-globulin, absolute or relative to the albumin level."

It would be interesting to know exactly how the results of many different tests yielding positive reactions due to the state of the blood colloids would compare when all were made simultaneously on the specimens of blood of a large series of cases. It is possible that a comparison of the results obtained by testing the same blood in numerous ways would give information of a different sort than that derived from any one test, such as the rate of sedimentation of red blood cells, the influence of serum on neutral red, methylene blue or Botelho's reaction. A specific reaction for cancer or some other noninfectious disease, as suggested by Wells,¹⁵ may possibly in time be developed along lines of research concerning the physical state of the blood colloids.

CONCLUSIONS

Botelho's reaction is of no value in the diagnosis of cancer.

It depends, like many similar tests, on some change in the physical state of the blood colloids, and may give positive results on serums from patients suffering from any disease condition in which there is such a change.

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General Review

PARASITIC INFECTIONS AND HUMAN DISEASE IN CHINA *

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Since the days when Sir Patrick Manson carried on his investigations in Amoy and Hongkong, China has been known as a country of unusual interest and opportunity to the student of parasitology and tropical medicine. Workers from several Western institutions have made special trips to China to study certain infections. A much larger group of medical men from the West, serving in the capacity of port health officers or in mission hospitals, has been confronted with patients suffering from various parasitic infections. In attempting to combat such diseases, these men have contributed to the knowledge of the diseases in question and to the life histories of the causative organisms involved. It is now known that the number of animal parasites of man in China is as large and the distribution is as extensive as in any other part of the world.

Because of the importance of parasitic infections in China and the Far East, I have been asked to review the more important investigations in parasitology that have been carried on in China during the last few years. These include studies (1) on the distribution of parasitic diseases in China and (2) on the biologic, epidemiologic and pathologic aspects of the most important disease-producing organisms of the area.

FACTORS INVOLVED IN THE STUDY OF PARASITIC INFECTIONS IN CHINA

A knowledge of the important physiographic features of the country, of the rainfall and of the climate is essential to an understanding of the extent of human parasitic diseases in China and to an appreciation of the enormous distribution of some of these infections. Many of them have intermediate hosts which serve to incubate the parasite during its larval stage. Others have reservoir hosts which perpetuate the life cycle when man purposely or unintentionally escapes the infection. To these facts must be added a consideration of the habits of the Chinese people which are primarily responsible for maintaining the human infection.

* Contribution no. 71 from the Parasitology Laboratory, Department of Pathology, Peking Union Medical College.

Physical Factors Involved.—China proper lies between the 20th and the 40th degrees north latitude and between the 100th and the 120th degrees east longitude. The country is dissected by four important river valleys, with a general west to east course, i. e., from the mountains and table lands of Central Asia to the sea coast. Beginning at the south these rivers are as follows: (1) the Hung Kiang (Red River), draining a part of Yunnan Province and spreading out into an extensive delta in Tonkin (French Indo-China); (2) the Chu Kiang (Pearl River), with its three extensive branches (the West River, North River and East River), providing drainage for the southeast provinces and emptying through the Canton delta; (3) the Yangtze Kiang (the River of Many Branches), with its principal sources in the mountain regions of the west and its delta near Shanghai (this is by far the most important river system of China and occupies the same position here that the Mississippi River does in North America); and (4) the Huang Ho (Yellow River), which has its sources in the far northwest and which, after a devious course through the plateaus and plains of the north, finally empties into the Gulf of Pechihli (see chart).

Various mountain ranges along the coast as well as extensive mountain systems in the provinces of the hinterland further modify the configuration of the country and serve as physical and biologic barriers.

The rainfall is heaviest in the south and decreases toward the north. The season of heavy rainfall also extends over a longer period in south China than in north China. This has a definite bearing on all life. North of the Tsing Ling Range and Fu Niu Mountains rainfall averages less than 75 cm. per year, which is not enough to propagate many helminth infections that flourish further south, so that clinical cases of these infections are seldom seen to the north of this mountain system.

The season of favorable temperature for the propagation of parasitic infections exists practically throughout the entire year in the Yangtze valley and to the south, except in the high mountain areas. To the north of the Yangtze Valley the season corresponds to the period of rainfall.

With these points in mind, it can be readily understood why many infections of clinical importance are confined to central and south China, while the significant diseases of north China are those that can survive drought and cold.

Importance of Intermediate and Reservoir Hosts in Perpetuation of Animal Parasites in the Orient.—The student of medicine in the West is familiar with the rôle which the pig plays as intermediate host in trichinella and pork tapeworm infections and that which various fresh water fishes play in the propagation of the broad fish tapeworm, *Diphyllobothrium latum* (*Dibothriocephalus latus*). The consumption by the population of the Orient of an infinite variety of animals and plants strange to the western palate has been responsible for the transfer to

man of many parasitic infections which are peculiar to the Orient and which are a result of such food habits. Raw foods which harbor larval stages of these infections or foods contaminated with diluted night soil are always subject to suspicion in China and other parts of the Orient.

One important group of disease-producing organisms (the trematodes or flukes) requires as an intermediate host a snail which is specifically adapted to each type of fluke. In China and in the adjacent areas there are eight or more species of this group of metazoa which are parasitic in man. One of these species (the Oriental blood fluke)



Nosographic map for animal parasites of man in the Sino-Japanese area.

penetrates the mammalian skin soon after emergence from the snail in which it first develops; others require a second intermediate host in which the infection must be incubated before the organism is infective for man. In the latter type of life cycle the common method of human infection consists in the consumption of the second intermediate host either raw or insufficiently cooked.

Various mammals and sometimes even birds may harbor the same stage of a fluke infection found in man. In any area such as China

where such infections are common, it is necessary, in order to act intelligently, to know not only the incidence and distribution of the infection in man, but also to have at one's disposal similar data from domestic mammals, their wild relatives, as well as other animals which might and frequently do serve as reservoir hosts of the infection. In certain of these diseases in China (for example, oriental schistosomiasis) man is the only important host involved; in others (for example, fasciolopsiasis, clonorchiasis and Manson's tapeworm infection) the pig, the dog or the cat are important reservoir hosts responsible for the propagation of the life cycle; in still other instances, man incurs the infection only incidentally (for example, infections with various nematodes commonly found in ruminants, such as *Trichostrongylus orientalis*).

Conditions Responsible for Propagation of Parasitic Diseases in China.—The most usual method by which parasitic infections are dispersed is by pollution of water and of food with night soil. The economic system in China requires that human night soil be returned to the land. By this means, and by promiscuous defecation of man and of domestic animals serving as reservoir hosts, and by uncleanly personal habits, man has become infected and has perpetuated and increased the amount of the infection. Where the disease is not incurred by direct contamination, food products consumed raw serve as a *via major* for transmitting the infection to man. Under such circumstances differences in the food habits of the different provinces or even climatologic differences serve to check infections that would otherwise be widespread throughout the country.

Relation of Contiguous Areas to the Parasitic Diseases in China.—The area of protozoan and helminthic infections in south China imperceptibly blends into that of French Indo-China. The parasitic diseases of Kwangtung Province and of Tonkin are remarkably alike, while those of Annam, further to the south, show a perceptible difference. Likewise, the diseases of Formosa differ only quantitatively from those of the adjacent coast of China, while at least the helminthic infections of Japan and Korea are comparable to those of the Yangtze valley. Two infections peculiar to the Sino-Japanese areas (*schistosomiasis japonica* and *paragonimiasis*) have even been reported to be endemic in the Philippines. It is evident, therefore, that the factor of contiguous areas enters intimately into a consideration of the distribution of parasitic diseases in the Orient.

Methods of Working Out Nosogeography of Parasitic Diseases.—The first attempt to compile data on the distribution of parasitic diseases in China was made by the Research Committee of the China Medical Association which, through questionnaires and correspondence, collected preliminary data, afterward published by Jefferys and Maxwell in

"Diseases of China." Within more recent years it has seemed advisable to undertake more intensive investigations in certain typical areas of China, where surveys of the hospital populations and of healthy persons have been made, as well as extensive examinations of mammals, birds, amphibia, fishes, molluscs and arthropods, which might be found to serve as reservoir or intermediate hosts of human infections, or which might give a clue as to the development that certain groups of parasitic organisms had attained in certain typical areas. Such investigations have been carried on by Faust (1921), Young and Hertig (1926) and Kessel and Svensson (1924) in northern China, by Faust and Wassell (1921), and Li (1923) and Oppenheim (1925) in the central and lower Yangtze valleys, respectively, and by Cadbury (1914), Faust (1923) and Cort, Cadbury and Oldt (1925) in southern China. Western China still remains to be studied. In addition to these more general surveys, special investigations have been made on diseases of particular importance. Those on which reports have been published or are in press comprise the following: Faust and Meleney: Studies on *Schistosomiasis japonica*, 1924; Barlow: The Life History of *Fasciolopsis buski*, 1925; Cort, Grant and Stoll: Report of the China Hookworm Commission, 1926; Young and Hertig: Field Studies on Kala-azar, 1926; Faust and Khaw: Studies on *Clonorchis sinensis*, 1926.

HUMAN PARASITIC INFECTIONS IN CHINA

The animal parasites of man in China may for convenience be classed as those of major importance and those of minor concern. This classification is based partly on the clinical and pathologic importance of the organism and partly on the geographic extent of the infection.

The protozoan diseases of major importance in China are malaria, amebiasis and kala-azar. The helminthic infections belonging to the same category are oriental schistosomiasis, clonorchiasis, fasciolopsiasis, hookworm infection and filariasis.

Protozoan Diseases.—Malaria: Malaria is found throughout China, from the extreme south as far north as Peking, and from the coast to western Szechuan Province. In general, malaria is most severe in the south and is progressively less important toward the north, while it is entirely unknown as an endemic infection to the northwest of Peking. The incidence, therefore, conforms on the whole to the amount of rainfall for these respective areas. The islands of Hainan and Formosa and the adjacent coastwise country of the mainland and the Yangtze valley are all heavy endemic areas. It would be a mistake, however, to assume that this entire territory is equally heavily infected. Recent questionnaires which I sent out in connection with the activities of the Research Committee of the China Medical Association, inquiring

into the present incidence of malaria, the species of parasite present, and the species of anopheline hosts involved, serve to illustrate this point.

There are spots of great infestation throughout central, south and west China. In certain areas there is an incidence of from 90 to 100 per cent, yet within a radius of 100 miles from such centers malaria is seldom observed. The reason for this has not yet been worked out. All three species, *Plasmodium falciparum*, *P. vivax*, and *P. malariae*, are found throughout the malarious stretches of China. The subtertian species appears to be more common in the south, while the quartan species is usually found in the Yangtze valley. Yet all three species occur in the extreme south, just as in French Indo-China and in the Malay States, and, likewise, all three occur in northern China (Peking). One species may occur as a heavy infection in one area while another species is the predominant one twenty-five miles away. The areas from which infected patients come to certain medical centers for treatment are frequently recognized by the species of malarial infection which they harbor. Furthermore, the extensive travel of merchants, students and soldiers from one area to another has spread the infection from one area to another, particularly from the south to the north.

Another point of interest epidemiologically in malarial infection in China is the range of the anopheline mosquitoes capable of transmitting the infection. China lies in two biologic regions, the Palearctic and the Oriental (Faust, 1925). In north China, *Anopheles* (*Anopheles maculipennis*), the species common in Europe and extending through Siberia to North America, is the common form available to transmit the infection. In central and south China, several species are probably involved, including *Anopheles* (*Myzorrhynchus*) *sinensis* and *A.* (*Myzomyia*) *ludlowi* of the oriental fauna, and *A.* (*Nyssorrhynchus*) *maculatus* of the Australian fauna.

Clinically it is important to note that blackwater fever is unknown in China, except in Yunnan (Red River and Mekong River drainage), where Mason (1924) has recently seen cases.

Amebiasis: Amebiasis, with both primary and secondary manifestations, is found throughout China. However the incidence of acute amebic dysentery and of "carriers" differs considerably in different areas and in different populations. In Wuchang (central Yangtze valley) Faust and Wassell (1921) found 50.9 per cent of the hospital population positive for the dysentery ameba, of which group 15.9 per cent had amebic dysentery while the remainder (35.0 per cent) were "carriers." A healthy Chinese group at Kuling showed 10.8 per cent infection in which cysts only and no trophozoites were found. On the other hand, a representative foreign population at Kuling had an incidence of 21.4 per cent of acute or chronic amebic colitis, while in only 6.1 per cent

were the cysts alone found. More recently Faust (1924), Kessel and Svensson (1924) and Kessel and Willner (1925) have studied groups of native and foreign residents of Peking. Of ninety-six Chinese and thirty-three foreigners whose tests were positive for *E. histolytica* between Oct. 1, 1923, and June 1, 1924, 19.8 per cent of the former and 30 per cent of the latter had either definite symptoms of amebic colitis or secondary symptoms; 35.4 per cent and 9 per cent, respectively, were healthy "carriers," while the remainder showed symptoms of disturbed digestion that might have resulted from mild amebic colitis. Recently in several hundred cases of Chinese hospital patients and school children in Canton whom I examined in midwinter, 1925 (unpublished data), only two cases of *E. histolytica* "carriers" were found, although the number of cases of acute amebic dysentery constituted 10 per cent of the total group examined. These data when considered as a whole support the view that in a given Chinese population a relatively larger proportion of acute amebic infection is to be found in the south while a higher percentage of "carriers" is present in the north. Furthermore, the incidence of acute or chronic cases of amebiasis appears to be higher in foreign residents in China than in the native population. The danger of the "carrier" to the community remains to be demonstrated.

Clinical studies of amebic infections in China (Kessel and Willner, 1925) have shown that yatren is effective in clearing up stubborn chronic cases and "carriers," but that emetin is the drug of choice in acute amebic dysentery.

All of the amebas described from other areas where surveys have been carried on have been found in China, but none of them has been shown to be of clinical significance.

Kala-azar: Kala-azar or visceral leishmaniasis is an important disease in parts of north China. First described from this area in 1904, its significance has been increasingly recognized in certain clinics. The recent survey of Young (1923) confirms the earlier one of Cochran (1911-1913) to the effect that the disease is confined to the territory north of the Yangtze valley, the heaviest incidence being found in northern Kiangsu, eastern Anhwei, Shantung, Chihli and eastern Shansi provinces. The presence of the infection in Shensi and Kansu provinces (northwestern China) has given support to the hypothesis that the disease may originally have been introduced into China along the north-western trade route.

Young and Vant Sant (1923) have shown that cultures of peripheral blood and even smears prepared after centrifugalization of peripheral blood may be used for the diagnosis of Leishman-Donovan bodies in suspected cases of kala-azar. However, cultures from spleen puncture have been found, on the whole, to yield more satisfactory results.

The striped hamster, *Cricetulus griseus*, and the giant hamster (*C. triton*) have been found to be excellent laboratory animals for the infection (Young, Smyly, Brown, 1926; Young and Hertig, 1926). But field studies by Young and Hertig (1926) and Young and Liu (1926) have failed to show that these rodents carry the infection in areas where the incidence in man is heavy. While rodent lice and bedbugs ingest kala-azar bodies along with a blood meal taken from infected hosts, there is no evidence that these insects actually transmit the infection.

Sia (1921, 1924) and Sia and Wu (1921) have shown that Ray's "hemolytic test" in kala-azar is indicative of an increased serum globulin in the blood. These workers have emphasized the value of the precipitation reaction in diagnosis. Antimony treatment has proved satisfactory in the treatment of kala-azar in China.

Other protozoan infections common in China are the intestinal flagellates and ciliates, and the spirochetes of relapsing fever and of broncho-spirochetosis.

(a) Intestinal flagellates are found throughout China just as in other parts of the world. Their clinical significance is still poorly understood. The flagellate forms range all the way from species considered to be definite tissue parasites to those which are purely contaminations. *Giardia lamblia* is believed to attach itself to the intestinal mucosa and in so doing causes erosion and catarrh of the mucosa. *Chilomastix mesnili* and *Trichomonas hominis* are probably not parasitic, but their presence may indicate an abnormal condition of the intestinal pH . *Cercomonas* and *Bodo* are definitely coprozoites.

(b) Balantidiosis occurs in pigs in China but is not reported from man.

(c) Relapsing fever breaks out sporadically in central and northern China, Manchuria and western China. It occurs most frequently in the spring. The body louse is undoubtedly the vector in northern China. since delousing experiments have eliminated 95 per cent of the infection (southern Chihli province, Famine Relief Commission data, 1920-1921).

(d) Various workers have described the bronchial spirochete in China. Faust (1922) recorded typical cases from the Yangtze valley and demonstrated its importance in uncomplicated infections and in patients with pulmonary tuberculosis.

Metazoan Diseases.—Schistosomiasis japonica: Oriental schistosomiasis was discovered in China by Logan (1905) soon after the identification of the causative organism, *Schistosoma japonicum*, by Katsurada (1904). Since that time the disease has been found in various centers in the Yangtze valley. A study of the problem in the field and in the laboratory by Faust and Meleney (1924) has contributed the following facts to the knowledge of schistosomiasis japonica in China.

The disease is found throughout the Yangtze valley, including the three large lakes (Tai Hu, Po Yang and Tung Ting) and the Grand Canal system in the lower Yangtze. It also occurs in small areas along the coast as far south as Hongkong, and in the North River country above Canton. Recently Cullen (1924) has seen cases from southern Yunnan province, in the upper Mekong drainage.

Throughout the Yangtze valley the intermediate host is *Oncomelania hupensis*, a small amphibious snail, which lives along the banks of quiet canals and backwaters and avoids large bodies of water. In the coastal mountain streams the intermediate host is *Katayama nosophora*, a closely related snail. The disease is contracted primarily by farmers in the rice nursery beds and by river boatmen, the infective larva penetrating through the skin of those parts of the body exposed to "infected water." Probably one hundred million people are endangered by the infection. In China man is the only important definitive host.

Early in the disease there is an urticarial rash, followed by a high eosinophilia and increased blood serum globulin. The seat of the adult worms is in the hepatic portal vessels, the worms having reached this region by migration through the blood stream. The presence of the worms and of their eggs, which are extruded into the portal capillaries and into the tissues of the liver and the intestinal wall, gives rise to dysentery, thickening of the wall of the intestine and hepatic cirrhosis with accompanying ascites. Antimony therapy is specifically indicated for schistosomiasis japonica, but Meleney, Faust and Wassell (1925) have shown that care should be exercised in treating advanced cases. Ultimate eradication of the infection from endemic areas can come about only through sterilization of night soil.

Clonorchiasis: Clonorchiasis is the most important of the fluke infections in China contracted through the consumption of raw fish. The disease occurs in cats and dogs in all parts of China except in the northwest provinces, but human infection is confined almost exclusively to Kwangtung province, where in the regions of Canton and Swatow, it is of clinical significance (Chen Pang, 1923, 1925; Faust, 1925). In this area from fifteen to twenty million people periodically subject themselves to infection with this fluke. This first intermediate host is the snail *Bythinia striatula*. Later, fresh water fishes are utilized by the worm. Faust and Khaw (1926) have shown that practically every fresh water fish in China is capable of serving as second intermediate host. The fishes harbor the encysted larvae and transfer them to the definitive (mammalian) host unless cooked thoroughly.

The parasite lives in the bile capillaries and the bile ducts. In cases of light infection only the smaller, more distal capillaries are occupied, but in heavier infections the larger vessels are also filled with the worms.

Most of the human cases outside of restricted endemic areas in Kwangtung have only a light infection (less than fifty worms), which, however, may persist for many years. In mild infections there is no noticeable clinical symptom. Constipation and indigestion may possibly accompany such an infection, due to interference with normal bile flow. In heavy infections, however, the pathologic process is more involved. In addition to proliferation of the biliary epithelium there is extensive fibrous connective tissue formation and amyloid (?) deposition around the bile passages which have become greatly enlarged to accommodate the parasites, leukocytic infiltration around extravasated ova of the parasite, and later involvement of the hepatic veins. This process begins in the more distal superficial bile capillaries where the worms are most commonly found, and becomes more and more extensive until a lobe of the liver or even the whole organ is involved in a general cirrhosis. In these advanced cases icterus develops; in late cases ascites is common.

In experimental therapy on cats, Faust, Yao and Khaw (1926) have proved that mercurochrome in doses toxic to the host is not clonorchicidal. On the other hand, cures have been effected in experimental animals by the oral administration of gentian violet (Grübler), and the hosts have remained healthy and gained weight. Prevention of the disease can be effected through educating the population to cook all fresh water fish thoroughly.

Paragonimiasis: This disease (endemic hemoptysis or pulmonary distomiasis) is most common in Korea and Formosa, but cases of the disease are reported from Fukien province and from the Yangtze delta. Faust (1922) has found the infection in the first intermediate host, the snail (*Melania ebenina*), in the central Yangtze valley. It is not common in man on the mainland of China.

Other flukes of minor importance in the Sino-Japanese areas, infections of which are contracted by mammals through consumption of raw fish are the following: *Opisthorchis felineus*, *Metorchis* sp., *Metagonimus yokogawai*, *Heterophyes* (probably three species), *Stamnosoma* (two species) and *Pygidiopsis genata* (Faust and Nishigori, 1926). Both *Opisthorchis felineus* and *Metorchis* sp. are parasitic in the bile passages. The other forms, all belonging to the family *Heterophyidae*, are attached to the intestinal mucosa. *Opisthorchis felineus* is of clinical importance in Russia and Siberia. The few cases reported from China thus far have been among the Russian population. *Metorchis* has been found only in cats (Shanghai, Peking) but is a possible parasite of man. All of the other forms are intestinal parasites of man and mammals in the Far East. Some of them are common in dogs and cats in China and are occasionally found in man. In human cases they give rise to intestinal disturbances with excess of mucus in the stool. *Heterophyidae* can all be successfully treated with carbon tetrachloride.

Fasciolopsiasis: This infection is due to the presence of the large fluke, *Fasciolopsis buski*, in the small intestine. It is found in man and in the pig in central and south China and in Formosa, and is reported from the Chinese and Indian (?) population in the Malay and in parts of British India. I have recently discovered the dog as an important reservoir host of the infection in south China (Siulam, Kwangtung province). The areas of heavy human infection are in northern Chekiang province (Shaohsing) and in Kwangtung (Canton and Siulam).

Barlow (1925) has carefully worked out the life cycle of the fluke for the heavily infected district of Chekiang province, which covers about 1,600 square miles, where "the disease profoundly affects the life of between a million and a million and a half of people, reducing their efficiency and causing great loss of life." The first intermediate hosts are the snails, *Planorbis schmackeri* and *Segmentina nitidellus*. Man incurs the infection through eating raw water chestnuts (*Eliocharis tuberosa*) and the water caltrop (*Trapa natans*), on the skin of which the larval flukes become encysted (Barlow). Pigs are infected by foraging in fields for these bulbs. Severe infections give rise to definite clinical symptoms, with fulness of the abdomen, constipation, dyspepsia, edema of the face and lower extremities, and anemia. Beta naphthol and carbon tetrachloride are specific therapeutics. Prevention of the disease can be brought about by immersing the infested bulbs in boiling water for a few seconds.

Fluke infections of importance in veterinary medicine, occasionally found in man in China, incurred through the consumption of raw plant products are as follows: *Fasciola hepatica* (the common liver fluke of sheep), found in sheep and cattle in central and south China and in camels in north China; *Fasciola gigantica* (the giant liver fluke) found in cattle and water buffaloes in central and south China; *Eurytrema* species, found in hogs in south China, cattle in central China and camels in north China; and *Dicrocoelium dendriticum* (the lesser sheep liver fluke), found in sheep in north China. Occasional cases of these infections in man are reported, but such records are rare. *Watsonius watsoni*, reported from tropical Africa as a human parasite, is occasionally found in monkeys in China.

Hookworm: Ancylostomiasis has been known for many years to be an extensive helminthic infection in China. In 1917, the International Health Board compiled a reference list of 100 sources of published data and forty more of correspondence relative to hookworm disease in China. Hospital reports from central and south China have shown especially heavy infestations in these respective areas, while careful laboratory examinations in north China (Peking, Chefoo) have dem-

onstrated an unexpectedly high incidence (20 to 38 per cent). In north China it has been noted, however, that clinical infestations seldom occur.

In order to investigate the underlying biologic facts relative to hookworm disease in China, the China Hookworm Commission (1923-1924), cooperating with the Peking Union Medical College, has recently studied the problem. Their findings (Cort, Grant and Stoll, 1926) confirm the observations of previous workers, in that hookworm is not a clinical entity in north China (in areas with less than 75 cm. yearly rainfall). In typical centers in central and south China (Soochow, Canton) this commission has found that the mulberry areas are the primary source of infection, while the rice fields are of little importance in the propagation of the disease. Stoll and Tseng (1925) have shown that after eliminating other possible factors, anemia is a definite accompaniment of heavy hookworm infestation, and that the hemoglobin percentage is correlated inversely with the number of hookworms present. Svensson (1925) has shown that there are morphologic distinctions in the mature filariform larvae of *Ancylostoma* and *Necator* which permit the laboratory worker to estimate accurately the relative proportion of these two larvae in stools or in polluted soil in an infected area. She has also demonstrated (1925 a) that the optimum temperature for the development of *Necator* larvae is considerably higher than that for *Ancylostoma* larvae, and that soil polluted with these two species may remain infective for at least fifteen weeks at any temperature between 2 and 38.5 C.

Filariasis: Filariasis in China was first called to the attention of the medical world when Sir Patrick Manson (1877-1883), working in Amoy, demonstrated nocturnal periodicity of the larvae of *Filaria bancrofti* in man and the metamorphosis of the larvae in the mosquito. Scant attention has been paid to filarial infection in China, although it is known to extend along the coast from the Tonkin border to southern Shantung, and up the Yangtze valley as far as Ichang (western Hupeh). Maxwell (1921) has published an extensive paper on clinical filariasis, lymphatic obstructions and inflammatory processes of the lymphatics in south China, but in many of his cases filariae were not demonstrated. C. U. Lee has recently studied the problem in northern Kiangsu province.

An ocular filaria (*Thelazia callipaeda*) is frequently found in dogs and cattle in China and has been described in man (Houghton, 1917; Stuckey, 1917).

Ascariasis: *Ascaris lumbricoides* is the most common human parasite in China, having been found in all regions in relatively large percentages of cases. Kessel has found (Mills, Bartlett, Kessel, 1925) that hypochloride of lime in ordinary solutions is not toxic to *Ascaris* eggs and that sterilization of raw fruits and vegetables can be accomplished only by their immersion in boiling water.

In the native population *Ascaris* seems to produce no special symptoms unless it migrates into unusual passages and causes occlusion of the bile tracts or inflammatory processes (appendix vermiformis). Except in emergencies, the routine procedure has been adopted throughout the Far East that all patients requiring abdominal operations shall first be freed from *Ascaris*. Oil of chenopodium or santonin is usually the prescribed therapy.

Trichuriasis: *Trichuris trichiura* is only less common in central and south China than *Ascaris* and hookworm. It is relatively uncommon in north China. Except in heavy infections it is not considered of clinical importance.

Gnathostomiasis: *Gnathostomiasis externa*, or creeping disease, has been reported in eight persons in the Orient, four of whom are from China (Morishita and Faust, 1925). The infection is caused by immature individuals (in most cases, *Gnathostoma spinigerum*) migrating through the subcutaneous tissue or lodged in cutaneous nodules. In central and north China I have occasionally seen the adult worms which live in tumorous nodules of the stomach of cats and dogs (*G. spinigerum*) and of hogs (*G. hispidum*).

Tapeworm Infections: *Taenia saginata*, the beef tapeworm, occurs in both the foreign and the native populations in China and is fairly common in north China (Mills, 1924), where cattle are imported from Mongolia. *Taenia solium*, the pork tapeworm, occurs endemically in at least three separate districts in central and north China. *Echinococcus* infection is found in Mongolia, and has been introduced into northern China. Its occurrence in other parts of China is rare. Only the unilocular type has been observed, usually producing hydatid cysts of the liver, but one case from the spleen and one from the orbit are on record among the Peking Union Medical College Hospital case reports. After several years of negative findings, I recently (1924) found the adult *Taenia echinococcus* in two Peking dogs.

In 1881, Manson (1883) found larval tapeworms in the abdominal cavity, pleural cavity, and in the flanks and iliac fossae during a necropsy at Amoy, in southern China. Cobbold examined them and named them *Ligula mansoni*. In 1919 Okumura published a study on the life cycle of this form, and demonstrated its genetic relationship to the genus *Diphyllobothrium*. The immature worm, which has been recorded several times in man in China and Japan, is common in the subcutaneous tissues and fascia of frogs and snakes throughout the Sino-Japanese areas. The adult worm, which resides in the small intestine of man, the cat and the dog, is more common in man in China than is the larva. The related tapeworm, *Diphyllobothrium latum* (*Dibothriocephalus latus*), is not known to be endemic in China, but cases have been introduced from Europe, Siberia and northern Japan.

Dipylidium caninum and *Hymenolepis nana* have been found in man in China but are of no special clinical significance.

THE NOSO GEOGRAPHIC AREAS OF CHINA AND THE FAR EAST

For convenience in visualizing the regional distribution of human parasitic diseases in the Sino-Japanese areas, the data which I have compiled from my investigations and observations have been graphically recorded on the accompanying map. The countries under consideration fall into five faunistic regions, which may be described as follows: (1) tropical oriental, (2) subtropical oriental, (3) intermediate, (4) palearctic, and (5) dry palearctic.

The tropical oriental region includes French Indo-China and the south China littoral as far north as central Fukien, together with the islands of Hainan and Formosa. The dominant parasitic diseases of the area are malaria and acute amebiasis. Clonorchiasis, fasciolopsiasis, hookworm disease, ascariasis, trichuriasis and filariasis are also commonly found in the area.

The subtropical oriental region is much more extensive than the former one, including the central and lower Yangtze valley, the China littoral from Fukien through Kiangsu province, and the southern half of Korea and of Japan. The southernmost portion of this area overlaps the tropical oriental region in Fukien and Formosa, where the two faunas are coextensive. The dominant infection of this region (exclusive of Korea) is oriental schistosomiasis, while paragonimiasis is a subdominant disease, particularly in Formosa, Korea and parts of Japan. Amebiasis, hookworm infection, ascariasis and trichuriasis are common.

Malaria is extensive throughout this region. In the tropical oriental region malaria is carried by anopheline mosquitoes belonging to the Oriental and Australian distribution; in the subtropical oriental region the mosquitoes are oriental and occasionally palearctic in type.

The intermediate region is one in which the oriental and palearctic regions meet. It is a region of moderate or abundant rainfall, of moderate or high altitudes. There is no dominant infection in the region. A certain amount of both oriental and palearctic infections occurs here.

The palearctic region includes the cold semi-dry region of north China and Manchuria and the cold regions of Korea and northernmost Japan. On the mainland of China the dominant infection of the area is kala-azar. In northern Japan the region resembles Siberia and the adjacent palearctic Russian zone, where diphyllorhynchiasis lata is common. Malaria, which occurs endemically in this region, appears to be carried by the palearctic species of *Anopheles* (*A. maculipennis*).

The dry palearctic region includes the arid upland plains of north-western China and Mongolia. Due to the dryness of the area the

dominant feature is the absence of all infections except occasional cases of kala-azar, ascariasis and echinococcosis.

In addition to its theoretical value, the practical importance of such a regional map showing the distribution of parasitic infections, has been demonstrated from time to time in the diagnosis service of the Peking Union Medical College Hospital. In cases in which residence is not known the diagnosis of certain infections frequently identifies the individual as a native of a particular zone. For example, schistosomiasis in a Chinese almost always means residence in the Yangtze valley; paragonimiasis, in Fukien, Formosa, Korea or Japan; clonorchiasis, in south China. Cases of clinical hookworm, particularly those with a high *Necator* index can usually be traced to central or south China. Kala-azar is referable only to north China.

COMMENT

It has been impossible to more than sketch the development that has taken place in the field of parasitology and tropical medicine in China during the last decade. Enough has been said, however, to indicate that both the clinician and the laboratory man are obliged to consider as important diseases produced by animal parasites which are peculiar to the Far East, diseases in many instances incurred by man due to customs peculiar to the Orient. Nowhere else in the world is the investigator confronted with so extensive a country, having such extreme variations in humidity and temperature, with such a formidable group of parasites in man and reservoir hosts, and yet having a single race of people on which the effect of the variations of these several factors may be studied. While the parasitic indexes of the populations of various districts in China have undoubtedly been modified from time to time, conditions as a whole are still essentially what they were two or three thousand years ago.

If one may judge from the differences in the reaction of the native population and of foreign residents in China who incur various parasitic infections simultaneously, the native is a more suitable host for the parasite, since his reactions are less specific. On the other hand, there is no evidence, as far as the animal parasites of man are concerned, that the native is less liable to infection than is the foreigner. Furthermore, there seems to be adequate evidence for the belief that the parasite is often better adapted to the reservoir host, where such exists, than to the native population. Such a conception is not entirely speculative, but frequently allows one to see the problem of human parasitism in the large in a way which individual human cases do not permit.

A difficulty which confronts both the practitioner and the investigator in China where the range of possible animal parasites of man is so considerable, is that of the relative importance of the various species.

There is no doubt about the importance of malaria, acute amebic dysentery, heavy hookworm infection, or schistosomiasis. However, there are the "healthy carriers" of the dysentery ameba, the person infected with a small number of hookworms or *Clonorchis*, and the healthy carrier of *microfilariae*. In addition to these definite parasites of the human host there are the intestinal commensals and fecal contaminants, which must be diagnosed if only to be ruled out as possible causes of clinical symptoms. Likewise, in public health problems one cannot neglect the intermediate or reservoir hosts, together with the parasites which they harbor that are involved at times in human disease. Finally, the difference in reactions of various persons and races to a particular parasitic infection requires careful consideration.

Practitioners in China have appreciated the importance of the surveys and special investigations on parasitic infections that have been undertaken in recent years by the staff of the Peking Union Medical College and cooperating institutions, and have generously aided such investigations. While medical men in the West have had little direct contact with these problems, they have shown an increasing interest in the work.

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Notes and News

American Association for Medical Progress.—President Clarence C. Little of the University of Michigan has accepted the chairmanship of the lay advisory board of the American Association for Medical Progress, and Mr. Peter Kasius, for several years assistant director of educational work, U. S. Public Health Service, has resigned that position to become field secretary of this association, which is planning an extended program for the coming year. The American Association for Medical Progress is a national lay organization for popular education on the scientific foundations of modern medical practice and public health work, with central offices at 370 Seventh Ave., New York.

Discoverer of *B. pyocyaneus* Dies.—The death is announced of Dr. G. Gessard who in 1882 isolated *B. pyocyaneus* and showed the pigment of blue or blue-green pus is the product of that microbe (La Pyocanine, Thèse, Paris, 1882).

Death of Stoerk.—Oskar Stoerk, aged 56, professor of pathology and head of the institute of pathologic histology and bacteriology in the University of Vienna, has died from sarcoma. He was for many years the first attendant to Professor Weichselbaum. He described the double refracting fat in chronic parenchymatous nephritis and showed that the husky voice in cholera is due to waxy degeneration of the muscles in the vocal cords.

Appointments by Medical Fellowship Board of the National Research Council.—Dr. Florence M. MacDonald, assistant in pathology, John Hopkins University, has been appointed to a fellowship for work in neuropathology and neuro-anatomy with Professor Carl Huber in the University of Michigan or Professor C. Judson Herrick in the University of Chicago.

Dr. Hobart A. Reimann, assistant resident physician at the hospital of the Rockefeller Institute, has been appointed to a fellowship in pathology for work with Professor Anton Gohn in the German University at Prague.

Dr. Howard J. Shaughnessy, instructor in public health, Yale University, has been appointed fellow in bacteriology for work with Professor Edwin O. Jordan in the University of Chicago.

Fund for Cancer Research.—Mr. E. F. Holmes has bequeathed \$100,000 to the University of Chicago to further research on the problem of cancer; Miss Harriet F. Holmes, a daughter, has been associated with H. G. Wells and Maude Slye in cancer research at the university for many years.

Dr. Gay Visiting Professor to Belgium.—Frederick P. Gay, professor of bacteriology, Columbia University College of Physicians and Surgeons, has accepted an appointment as visiting professor to Belgium under the auspices of the Committee for Relief in the Belgium Educational Foundation. Dr. Gay will remain abroad during the next academic year, lecturing on immunity at the Belgian universities in Brussels, Ghent, Liege and Louvain.

Japanese Cancer Research.—The Japanese Society of Cancer Research has recently appointed three research members under its special research fund: K. Yamagiwa, emeritus professor in the Tokyo Imperial University; T. Ogata, professor of pathology in the Tokyo Imperial University, and W. Nakahara, associate pathologist in the Government Institute for Infectious Diseases.

Collective Investigation of the Status Lymphaticus.—The exact part, if any, which status lymphaticus plays in sudden death is the subject of investigation by the Medical Research Council and the Pathological Society of Great Britain and Ireland. Information on the weight and measurement of the thymus gland will be collected on a large scale. The objects are: (1) to establish, by a large series of weights and measurements, the standards of weight for age, and the proportion to body weight of the normal thymus at all ages; (2) to investigate closely the precise cause of death in persons dying suddenly from unexplained and trivial causes when the only apparent abnormality is the presence of a large thymus.

In order to promote these objects, a committee has been formed and investigators have been appointed in large centers to collect detailed records. Pathologists and physicians who perform necropsies are asked to cooperate. The cases in which information is desired especially are: (a) cases of sudden death in apparently healthy persons of any age, including deaths from accident; (b) all cases of death in persons of 15 years or over who have an apparently glandular thymus.

American Association of Pathologists and Bacteriologists.—At the annual meeting in Albany, Hans Zinsser was elected president; James W. Jobling, vice president; Frank B. Mallory, treasurer; and Howard T. Karsner, secretary, 2109 Adelbert Road, Cleveland. The next meeting will be held in Rochester, N. Y.

French Journal of Pathologic Anatomy Changes Name.—*Annales d'anatomie pathologiques médico-chirurgicales*, established in 1923, has been made the official organ of Société Anatomique de Paris and will publish the proceedings of this society. Accordingly, the name has been changed to *Annales d'anatomie pathologique et d'anatomie normale médico-chirurgicale*. Hereafter nine numbers will be published annually.

Syphilis Infection from the Cadaver.—The opinion that syphilitic infection cannot occur from handling cadavers must be corrected. Nine certain and seven probable infections from cadavers have been reported in the literature (Erich Hoffmann, *München med. Wchnschr.* 73:185, 1926). The small number is partly due to the tendency to keep such instances secret. Postmortem multiplication of spirochetes takes place in macerated fetuses, in bodies of adults or children with congenital syphilis, and in infected rabbits. The form and staining reactions are retained for a long time; it was possible to stain them with silver after 110 days in salt solution. Motion is retained from twenty-four to thirty-six hours. The virulence apparently lasts at least twenty-four hours, and maybe longer. Koch reported infection of a rabbit with syphilitic tissue after three days. Infection from cadavers is a possibility, and should therefore be guarded against by physicians and pathologists. At a recent meeting of the Society of German Physicians, in Prague, Dr. J. Löwy reported an instance of syphilitic infection through injury of the ring finger during the necropsy of a woman six hours after death. A chancre developed at the site of the injury, and later a severe form of syphilis.

Abstracts from Current Literature

Pathologic Physiology

STUDIES ON COMPENSATORY HYPERTROPHY OF THE THYROID GLAND. LEO LOEB, *Am. J. Path.* 2:19, 1926.

On the basis of a large number of experiments, it can be stated that potassium iodide does not prevent or diminish the hypertrophy of the thyroid gland in the guinea-pig, which follows extirpation of a great part of the gland. On the contrary, the average of hypertrophy was greater in the animals which received potassium iodide than in the control animals. The average hypertrophy was less marked in the summer months than that in experiments carried out during the winter.

FUNCTION OF THE AUTOGENOUS KIDNEY TRANSPLANT. KENJI IBUKA, *Am. J. Med. Sc.* 171:407, 1926.

The successful autogenous kidney transplant in the neck of the dog functions for months in a practically normal manner, coexisting with the normal kidney in the abdomen; it also maintains the life of the animal in good health for a fairly long time after the excision of the other kidney, while preserving its own functional activity. One transplanted kidney was in good condition four months after removal of the other kidney.

The neck can be used as a site for transplantation, and the kidney can be there utilized for the study of certain renal functions, as well as of the physiologic activity of the transplant itself.

Analysis of chemical constituents of urine from the transplant as well as various functional tests made on it, simultaneously with the investigation of the remaining normal kidney in the abdomen or after the removal of this sister organ, shows a fairly normal kidney function.

An apparently compensatory activity of the transplant is observed after ablation of the other kidney.

The extrinsic nerve supply to the kidney and the ureter plays a minor and unessential part in their function, as the transplanted kidney functions equally well in the new location, and the renal pelvis and ureter show even an increased peristalsis.

The ultimate failure of the function of these autogenous kidney transplants, which have been transplanted successfully in the neck and functioned a fairly long while, seems to be caused by hydronephrosis and infection, mainly incurred by mechanical insult in the new location.

These results of autogenous transplantation of the kidney may serve as a controlling experiment for renal transplantation of other kinds, such as the homogenous or heterogenous.

AUTHOR'S SUMMARY.

FUNCTION OF THE HOMOGENOUS KIDNEY TRANSPLANT. KENJI IBUKA, *Am. J. Med. Sc.* 171:420, 1926.

Homogenous transplantation of the kidney was performed and studied in fourteen pairs of dogs, the same surgical technic and postoperative treatment being carried out as in the autogenous transplantation of the kidney previously

studied and reported (*Am. J. Med. Sc.* **171**:407, 1926). No special consideration was given to the breed of, or relationship between, donor and recipient.

The function of the homotransplants in the neck, present with the kidneys of the recipient, was observed. This was found to continue for a few days (an average of three days) after transplantation and to end by necrosis or softening of the transplant shortly after the cessation of its function.

Chemical analysis, of specimens of urine and functional tests on the transplanted kidney proved that the homotransplant functioned similarly to the autotransplant for a limited time, but the function soon changed and finally ceased, contrary to the behavior of the autotransplant, which had recovered and assumed normal function at the corresponding period when the homotransplant failed.

In the functional tests with phlorhizine, carmine, and phenolsulphonphthalein the excretion of sugar and these dyes was observed in the specimens of urine from the homotransplant as well as from the recipient's kidneys. The test with phenolsulphonphthalein on the homotransplant showed that the elimination of the dye from the transplanted kidney varied according to nitrogenous constituents of urine from it, and the total amount of this dye eliminated by three kidneys during the first hour after injection was apparently greater than that eliminated by the recipient's kidneys alone before operation.

While all three kidneys were functioning, the nitrogenous constituents of the blood were reduced, but the chlorides and sugar in the blood were not changed. The urea nitrogen showed the most marked reduction, but the non-protein nitrogen and creatinin also were decreased.

The macroscopic, as well as microscopic, examination of the specimens of the homotransplant revealed that the transplanted kidneys were affected at first by nephritic changes of the parenchyma, such as cloudy swelling and degeneration of the tubular elements, and then by marked nephritic processes in the renal tissue, showing profound degeneration of glomerular and tubular elements with extensive interstitial infiltration of leukocytes and small round cells.

This great difference in the length of survival and in the functional behavior of the homotransplant, as compared with the autotransplant, in the experimental operations which were performed in the same manner, cannot be attributed simply to the surgical or mechanical factors of the operation, but probably is due to some underlying biologic factor in homogenous transplantation which is not as yet understood.

AUTHOR'S SUMMARY.

TOXEMIAS OCCURRING IN THE EARLY STAGES OF MENTAL DISEASES. H. D. McINTYRE and ROBERT NORRIS, *Arch. Neurol. & Psychiat.* **15**:341, 1926.

Cases of manic-depressive insanity, schizoid and confusional attacks were found to be accompanied by signs of systemic toxemia in that there was an increase of the blood urea nitrogen, decrease in the alkaline reserve, leukocytosis and fever. On disappearance of the symptoms, the blood chemistry became normal. The indicated treatment in these early cases is alkalis. The authors believe that acid toxins "crack" the lipoidal emulsion within the nerve tissue, and the resulting change has some bearing on the causation of the mental disease.

ROY GRINKER.

THE SPINAL FLUID IN EPILEPSY: A STUDY OF FIFTY CASES. H. PATTERSON and PAUL LEVI, Arch. Neurol. & Psychiat. **15**:353, 1926.

The authors find that the spinal fluid pressure is usually normal in epileptic patients, with a great rise during severe attacks and no change in mild attacks. The hydrogen ion concentration, albumin, globulin, chloride and urea determinations were normal. There was a low cell count and no permeability of the meninges to potassium iodide. The colloidal tests were often positive, with a gold curve similar to that found in cerebrospinal syphilis.

ROY GRINKER.

THE EFFECT OF THE SYMPATHETIC NERVOUS SYSTEM ON THE PERIPHERAL VASCULAR SYSTEM. W. B. MOSSER and K. P. A. TAYLOR, Arch. Surg. **12**:760 (March) 1926.

Using the temperature of the limb as an indicator, these authors found no appreciable change following periarterial sympathectomy. By injecting alcohol into the sciatic nerve in sufficient strength to cause motor paralysis, they produced a rise in temperature averaging 4.5 degrees, which subsided as motor function returned.

N. ENZER.

BASAL METABOLISM IN THE TOXEMIAS OF PREGNANCY. H. J. STANDER and C. H. PECKHAM, Bull. Johns Hopkins Hosp. **38**:227, 1926.

In the latter half of pregnancy there is a definite elevation in the basal metabolic rate and a return to normal at about the tenth day of the puerperium. The return is gradual and steady.

In pre-eclamptic toxemia the basal metabolic rate is slightly higher than in normal pregnancy. It returns to a normal level at about the fifteenth day of the puerperium.

Nephritic toxemia is associated with a basal metabolic rate of about + 33 before delivery. This figure is slightly higher than that for the pre-eclamptic group. The tendency for the basal rate in nephritic toxemia is to stay elevated for a longer time during the puerperium than it does in pre-eclampsia.

The basal metabolic curve for the eclamptic group is almost identical with the nephritic curve.

Basal metabolism determinations do not prove of any real help in differentiating between the various types of toxemias in late pregnancy.

In normal pregnancy, as well as in the different toxemias of pregnancy, there is some factor or factors which result in an elevated basal metabolic rate as term is approached, a gradual return to normal ensuing during the puerperium. It is probable that such factor, or factors, may have to do with the growing product of conception as well as with a slightly increased activity of the thyroid gland.

AUTHORS' SUMMARY.

BLOOD CHANGES DURING DIGESTION WITH SPECIAL REFERENCE TO UREA FORMATION. S. MORGULIUS, J. Biol. Chem. **66**:353, 1925.

The urea concentration in the blood of dogs after the portal circulation has been completely cut off and the liver extensively atrophied, is found to be exceptionally low, whereas the nonprotein nitrogen is only slightly lower than normal and the amino acid nitrogen is entirely normal. During the absorption

of protein digestion products, the urea nitrogen of the systemic blood frequently increases before the amino acid nitrogen, which may even fall below its normal value. The liver is the predominant organ for urea formation.

ARTHUR LOCKE

A STUDY OF THE RETENTION OF URIC ACID DURING FASTING. W. G. LENNOX, *J. Biol. Chem.* **66**:521, 1925.

Variations in the excretion of uric acid following the use of various purine-free diets do not mean variations in production, but, rather, variations in the amounts of uric acid retained in the blood and tissues.

ARTHUR LOCKE

THE EFFECT OF THE ADMINISTRATION OF CALCIUM SALTS AND OF SODIUM PHOSPHATE UPON THE CALCIUM AND PHOSPHORUS METABOLISM OF THYROPARATHYROIDECTOMIZED DOGS, WITH A CONSIDERATION OF THE NATURE OF THE CALCIUM COMPOUNDS OF BLOOD AND THEIR RELATION TO THE PATHOGENESIS OF TETANY. I. GREENWALD, *J. Biol. Chem.* **67**:1, 1926.

The calcium content of the plasma is normally maintained at a constant level by an equilibrium between inorganic calcium and an organic compound of calcium. The parathyroid hormone is necessary to the preparation of this organic constituent which resembles but is not identical with calcium citrate.

ARTHUR LOCKE

ANOXEMIA IN LOBAR PNEUMONIA. CHRISTEN LUNDGAARD, *Medicine* **4**:345, 1925.

In from 10 to 20 per cent of patients with lobar pneumonia disturbances in the respiratory functions of the lungs cause an abnormally low oxygen saturation of the arterial blood. This in turn gives rise to a decrease in the amount and tension of the oxygen of the capillary blood.

Through physiologic and pathologic investigations it is demonstrated that when a decrease in the arterial oxygen content (and consequently also in the oxygen content and tension of the capillary blood) exceeds a threshold of 15 to 20 per cent, a group of pathologic symptoms appears in normal individuals. The main symptoms are: Cyanosis, mental disturbances, abnormal irritation of the nervous centers in the medulla, particularly of the respiratory center, probably an impairment of the function of the muscular system, particularly of the myocardium.

The term anoxemia is in most instances used to indicate the condition characterized by these symptoms. In other instances anoxemia simply means the underlying pathologic condition, namely, the incomplete oxygen content of the blood.

An attempt has been made to show by analyses of different facts published in the literature that the various anoxemic symptoms in the main appear at the same threshold level of arterial oxygen unsaturation. The presence or absence of a cyanosis may therefore in most instances serve as a clinically useful criterion for the presence or absence of an arterial oxygen deficit extensive enough to give rise to other less characteristic anoxemic symptoms.

In pneumonia similar symptoms are frequent. A deeper analysis of these symptoms shows, first, that anoxemia probably plays a part in their develop-

ment; secondly, that anoxemia is to be looked on as only one of the causes of these symptoms. To what extent some of the most important functional disturbances in pneumonia, namely, dyspnea and heart failure, are caused by anoxemia and to what extent by other factors, is not known.

In a considerable number of pneumonic patients with abnormally low arterial oxygen saturation, treatment with oxygen inhalation has caused the abnormal oxygen unsaturation to disappear. At the same time the anoxemic symptoms, especially the cyanosis, have either disappeared or decreased in intensity.

AUTHOR'S SUMMARY.

SOME RELATIONS BETWEEN THE CONCENTRATION OF BLOOD CORPUSCLES IN VENOUS AND CAPILLARY BLOOD AND THE BLOOD PRESSURE OF DIABETIC PATIENTS.

H. F. ROOT, J. W. THOMPSON and R. R. WHITE, *J. Lab. & Clin. Med.* 11:405, 1926.

In certain patients with high diastolic blood pressure, the capillary count (red) was higher than the venous red count at night but lower in the morning. This reversed relation suggests capillary stasis at the end of the day and was more marked in patients with obvious vascular disease. Increases in venous pressure produce the contrary effect; namely, high venous count and low capillary count.

S. A. LEVINSON.

IMMEDIATE EFFECTS OF ROENTGEN RAYS ON LIVING ANIMAL TISSUES. J. G.

STEPHENS and H. FLOREY, *Brit. J. Exper. Path.* 6:269, 1925.

The possibility of ultraviolet fluorescence excited within the tissues by roentgen rays is considered by Stephens and Florey as a possible mechanism operating in the production of effects by roentgen rays. Contrary to the results obtained by previous workers, no immediate fall of blood pressure or alteration in respiratory rate occurs during prolonged irradiation. It is suggested that previous results are explicable as being due to electrical leakage, and not to the action of roentgen rays. A method for the insertion of abdominal windows is described. By means of these windows, no changes could be observed in the spleen or other abdominal viscera.

INSULIN AND GLUCOSE UTILIZATION: EFFECTS OF ANESTHETICS AND PITUITRIN.

C. G. LAMBIE, *Brit. J. Exper. Path.* 7:22, 1926.

The average rate at which the tissues remove glucose from the circulation in the decerebrate cat with the liver tied off is 0.15 Gm. per kilogram per hour. This rate is increased by 75 to 100 per cent by insulin in doses of 10 units per kilogram. When the liver is included and the splanchnics are cut, the rate of removal averages 0.6 Gm. per kilogram per hour. The rate at which the tissues remove glucose from the circulation when the liver is excluded is about the same under anesthesia as in the decerebrate preparation. The rate at which insulin accelerates the removal of glucose appears to be unchanged by the administration of anesthetics. Doses of pituitrin which are sufficient to prevent the fall in blood sugar under insulin in the intact animal fail to do so when the liver is excluded, and glucose is supplied at the rate necessary to keep the blood sugar level during the control period.

S. A. LEVINSON.

THE SIGNIFICANCE OF THE PHYSIOLOGIC FLUCTUATIONS IN NUMBER OF THE PERIPHERAL LEUKOCYTES. E. F. MÜLLER and W. F. PETERSEN, *Klin. Wchnschr.* 5:137, 1926.

The peripheries and splanchnic regions are closely allied in their autonomic vascular innervation. There is a splanchnoperipheral equilibrium, and the physiologic fluctuations in number of leukocytes in the same vascular regions represent delicate, compensatory changes in innervation.

ARTHUR LOCKE.

THE INTESTINAL WALL AS CO-REGULATOR OF THE p_H IN THE ORGANISM. W. LÖFFLER, *Klin. Wchnschr.* 5:179, 1926.

The stools become acid after an intravenous injection of sodium acid phosphate, while the acidity of the urine remains normal.

ARTHUR LOCKE.

THE IMPORTANCE OF THE CEREBROSPINAL FLUID FOR THE PATHOGENESIS OF UREMIA. E. BECHER, München. med. Wchnschr. 73:146, 1926.

Relatively large quantities of urea and uric acid, and some creatinin, go over into the spinal fluid during renal insufficiency, but intestinal putrefaction products are not found in the fluid so long as there are no truly uremic symptoms. The cerebrospinal fluid is intermediary in the metabolism of the brain, and when the barriers finally become permeable to protein degradation products, uremic coma ensues. There is no poisoning of the brain by these products in eclamptic pseudo-uremia. The pathogenesis of the latter symptoms is due to a mechanical disturbance consequent to cerebral edema.

ARTHUR LOCKE.

ANEMIA OF RATS FOLLOWING SPLENECTOMY. E. LAUDA, *Virchows Arch. f. path. Anat.* 258:529, 1925.

Although most animal species bear splenectomy well, a number of investigators have found that the rat is an exception in that it may develop a severe anemia to which it succumbs. Lauda found that 75 per cent of seventy-three splenectomized rats suddenly developed severe anemia, which reduced the red corpuscles to one or two millions within a day or two. Nine additional animals developed anemia but recovered. In eighteen the operation was not followed by any marked blood changes up to a period of thirty days after splenectomy. The anemia, which has been termed "pernicious anemia of rats," is characterized by those changes in the peripheral blood which are considered characteristic of pernicious anemia in the human being. The rapidly developing anemia is associated with moderate icterus, a positive direct and indirect van den Bergh reaction, hemoglobinemia and hemoglobinuria. Lauda considers the condition an acute hemolytic anemia. The most marked histopathologic changes were found in the liver and consisted of areas of focal necrosis of the parenchyma and of swelling of the reticulo-endothelial cells, which contained destroyed erythrocytes. The bone marrow showed little change; occasionally erythrophagocytosis by reticulo-endothelial cells was seen. Domagk had sought the explanation of the anemia in the erythrophagocytosis; Lepehne ascribed it to excessive activity of the reticulo-endothelial system. The sudden development of the anemia at variable periods after splenectomy, its hemolytic character, and its rapid course led Lauda to believe that the anemia was the result of infection. Injection of ground liver derived

from rats which had succumbed to the anemia, into rats which had withstood splenectomy as long as fifty days, was followed by anemia and death. It was possible to transmit the anemia causing agent through successive series of rats. Injection of heated liver suspension was not followed by anemia. Nonsplenectomized rats as a rule withstood the injection of the material. In three such animals, however, it was possible to cause anemia. From his results, Lauda concludes that pernicious anemia of splenectomized rats is due to a living virus to which splenectomized animals are much more highly susceptible than nonsplenectomized ones, and that the spontaneous occurrence of anemia in some splenectomized animals and not in others indicates that the virus is an endogenous one and is not one introduced at the time of operation. The exact nature of the virus was not determined and the relationship of the spleen to the development of the infection also remains in doubt, although Lauda supposes that the spleen, when present, by its immunobiologic properties protects the animal against all but overwhelming doses of the infection. He compares the disease of rats with the so-called "pernicious anemia of horses," and concludes that the latter is also infectious in origin, although the virus of one species is not transmissible to the other species. While he admits that the course of primary pernicious anemia of human beings is quite different from that of the anemia of rats and horses, he discusses the theoretic arguments which might favor an infectious origin of the human disease.

O. T. SCHULTZ.

TISSUE CULTURE. M. H. KUCZYNSKI, E. TENENBAUM and A. WERTHEMANN, *Virchows Arch. f. path. Anat.* **258**:687, 1925.

Kuczynski and his co-workers studied the effect of replacement of leukocytic, embryonic and bone marrow extracts by known chemical substances on cultures of tissues of half-grown guinea-pigs in the plasma of adult guinea-pigs. In spleen cultures they found that the addition of Witte's peptone and glycogen supported a rich growth of histiocytes and fibroblasts. Multiplication of liver cells under similar conditions could not be obtained. Glucose alone appeared to interfere with growth of liver tissue, but insulin set aside this inhibitory action. It was impossible to bring about a formation of agglutinin or hemolysin in tissue cultures.

O. T. SCHULTZ.

SECRETORY ACTIVITY OF THE NONGRAVID MAMMARY GLAND. L. LITTEN, *Virchows Arch. f. path. Anat.* **259**:126, 1926.

Litten made a histologic study of mammary glands of eighteen nonpregnant women in whom a milky secretion could be expressed from the nipple. In four of these the condition was due to simple retention after normal lactation. In five cases the phenomenon occurred during the menstrual or premenstrual stage and was associated with the acinar hyperplasia of the mammary gland which Rosenberg has described as a normal phenomenon of the menstrual cycle. In the remaining nine cases secretory activity bore no relation to the menstrual cycle and was noted especially in older women, some of whom had passed the menopause and whose breasts contained cysts or adenomas. For the last named group Litten proposes the term pathologic lactation, as contrasted with the postpartum retention lactation and menstrual lactation of the other two groups.

O. T. SCHULTZ.

Pathologic Anatomy

CONCERNING THE CONFUSION BETWEEN ACUTE LEUKEMIA AND INFECTIOUS MONONUCLEOSIS. H. P. SCHENCK and O. H. PERRY PEPPER, *Am. J. Med. Sc.* **171**:320, 1926.

It is important in hematologic reports to define just what is meant by the terms employed. Confusion has resulted from a failure to do this. Only by careful reports can the proper distinction between true lymphocytosis, acute lymphatic leukemia and infectious mononucleosis be made.

The syndrome agranulocytic angina apparently does not deserve to be considered a special entity but merely one type of reaction to serve infection.

A case of acute leukemia is reported, of the lymphatic or lymphoblastic type, in which during a remission, perhaps induced by treatment, the blood picture passed through stages at which it closely resembled infectious mononucleosis and even reached the stage where it resembled the picture of agranulocytic angina. A rapid return of the leukemic blood picture, however, followed with fatal outcome.

AUTHORS' SUMMARY.

BENIGN PERFORATING DUODENAL CYST ARISING FROM VESTIGIAL REMAINS OF WOLFFIAN BODY. M. E. VOGT, *Am. J. Obst. & Gynec.* **10**:798 (Dec.) 1925.

Vogt reports a neoplastic structure apparently originating from the remains of the wolffian body. A rounded, cystic tumor situated retroperitoneally communicated directly with the posterior duodenal wall and lumen by a firm, mushroom shaped growth, papillary in type. There were numerous, fluid-filled cystic spaces in the tumor, similar to those in cystadenoma of the ovary. The central portion of the neoplasm contained a number of glandlike spaces lined by columnar epithelium. Two of these could be traced to the main retroperitoneal mass.

A. J. KOBAK.

HISTOLOGIC INTERRELATIONSHIPS OF MENSTRUATION AND OVULATION. E. NOVAK, *Am. J. Obst. & Gynec.* **10**:802 (Dec.) 1925.

Novak reviews the histogenesis of the corpus luteum. The rupture of the mature graafian follicle, the development of the corpus luteum to its maximum, and then its retrogression are chronologically fitted into definite phases of the menstrual cycle.

A. J. KOBAK.

DELAYED CHLOROFORM POISONING FOLLOWING DELIVERY. G. D. ROYSTON, *Am. J. Obst. & Gynec.* **10**:808 (Dec.) 1925.

Three cases of delayed chloroform intoxication in patients having prolonged and difficult labor are reported. Operative intervention was necessary; the patients received morphine and scopolamine, and chloroform was used in all cases during delivery. The day following delivery the patients became jaundiced and vomited. Stupor and eventually coma followed some time later. In one case there was no coma until the seventh day. In two of the patients, the liver dulness was perceptibly decreased. One of these patients died, and at necropsy the liver weighed 950 Gm. and showed central necrosis of the lobules. Fat was increased in the center of the lobules just outside of the necrotic zone, but was scant in the periphery. The kidneys showed fatty degeneration, and the stomach hemorrhagic erosions. Infection was associated in all cases,

and in one a positive blood culture was obtained. The cases described were demonstrated to be in accord with the experiments of Graham, in that preliminary starvation and exhaustion had made the liver more susceptible to chloroform poisoning.

A. J. KOBAK.

AURICULAR ENDOCARDITIS OF RHEUMATIC ORIGIN. WILLIAM C. VON GLAHN, *Am. J. Path.* 2:1, 1926.

In the endocardium of the auricle, there occur lesions which are distinctive of rheumatic endocarditis both grossly and histologically. The endocardium of the left auricle is more frequently the site of the lesions than that of the right auricle. In the series of cases studied, the left auricle was involved in approximately one third of the cases of rheumatic valvular endocarditis.

AUTHOR'S SUMMARY.

A CASE OF RHEUMATIC AORTITIS WITH EARLY LESIONS IN THE MEDIA. ALWIN M. PAPPENHEIMER and WILLIAM C. VON GLAHN, *Am. J. Path.* 2:15, 1926.

The changes described occurred in the adventitia and the outer two thirds of the media. Here the endothelial cells of the vasa vasorum were swollen, and there were accumulations about the vessels of round and plasma cells and polymorphonuclear leukocytes. The appearances described support the view that perivascular scars in the media result from earlier inflammatory foci.

THE PERSISTENCE OF THE GLOMERULAR CIRCULATION FOLLOWING OCCLUSION OF THE RENAL VEIN OF ONE KIDNEY IN THE CAT. ISOLDE T. ZECKWER, *Am. J. Path.* 2:57, 1926.

The persistence of glomeruli with widespread necrosis of tubules following section of the renal vein of one kidney in cats indicates that the glomeruli have an independent circulation.

LIPOID-CONTAINING CELLS IN THE SPLEEN IN DIABETES WITH LIPEMIA. SHIELDS WARREN and HOWARD F. ROOT, *Am. J. Path.* 2:69, 1926.

Three cases of diabetes mellitus with large lipoid-containing cells occurring in the spleen are reported and compared with eight others collected from the literature. Lipemia is present in all the cases except that of Fahr and Stamm. The lipoid material in the cells, so far as can be judged from staining reactions, consists of cholesterol esters or related substances, or phosphatides. Fatty acids or soaps may also be present. The reticulo-endothelial system is probably involved in lipoid metabolism, and may perhaps selectively absorb cholesterol compounds or phosphatides. Arteriosclerosis appears to be associated with this condition. Lipemia, produced by a high caloric diet, by a poorly balanced diet or by the general cachectic state of the tissues in severe diabetes, may predispose to atheromatous degeneration in the arteries.

AUTHORS' SUMMARY.

ENCEPHALITIS PERIAXIALIS DIFFUSA OF SCHILDER: REPORT OF A CASE. S. BROCK, P. CARROL and LEWIS STEVENSON, *Arch. Neurol. & Psychiat.* 15:297, 1926.

The authors add one case to the thirty-two pathologic reports in the literature. There was a bilateral lesion of the white matter from the occipital region to the frontal lobe, the temporal lobes being least affected. The internal

capsule and corpus callosum were involved. The degenerated area was rough, gelatinous and dark gray. There was thinning of the very pale cortex. The axons were demyelinated except for the layers just below the cortex. The axis cylinders were relatively well preserved although also involved. Fat accumulations in the white matter stained with scharlach and osmic acid. Large perivascular globoid cells were present with single eccentric nuclei and granular cytoplasm which stained orange red with hematoxylin and eosin. There was marked neuroglial proliferation and new vessel formation. The ganglion cells of the parietal lobe were badly degenerated.

ROY GRINKER.

THE SPONTANEOUS ESCAPE OF CEREBROSPINAL FLUID THROUGH THE NOSE: ITS OCCURRENCE IN BRAIN TUMOR. C. E. LOCKE, JR., Arch. Neurol. & Psychiat. **15**:309, 1926.

The author reviews the literature and finds fourteen cases of spontaneous rhinorrhea. All were associated with internal hydrocephalus. Eight were tumors, two congenital hydrocephalus with rhinorrhea in adult life, two adult hydrocephalus and two of doubtful source. In eleven there was a communication between the floor of the anterior fossa of the cranial cavity and the nasal cavity. In seven the communication was between the cisterna basalis and the nose, in three between the anterior horn of the lateral ventricle and the nose, and in one there was a persistent lumen of the olfactory bulb. The fatal termination of ten cases was with purulent basal meningitis. The author reports two cases with necropsy. In one the communication was with the anterior horn and in the other with the anterior fossa.

ROY GRINKER.

THE PATHOLOGY OF JOINT TUBERCULOSIS IN ITS EARLIER STAGE. A. D. SMITH, Arch. Surg. **12**:740 (March) 1926.

This study is based on material obtained at operation on early tuberculous lesions of the joints. In twenty-three cases it was possible to determine the origin of the process, and in seventeen of these the synovial membrane only was involved. In three cases the metaphysis was involved without involvement of the joint. In the remaining three cases bone and synovial membrane were infected, the former more extensively. The development of the process when confined to the synovial membrane is much slower than in those with bone lesions.

N. ENZER.

CHRONIC NEPHRITIS PRODUCED BY ROENTGEN RAYS. J. R. O'HARE, H. ALTMAN, T. D. CHRISTIAN, A. W. CALHOUN and M. C. SOSMAN, Boston M. & S. J. **194**:43, 1926.

By exposing the kidney to the roentgen ray a progressive sclerosis may be produced.

A CLINICAL AND PATHOLOGIC STUDY OF TWENTY-SIX CASES OF DIABETES. HOWARD F. ROOT and SHIELDS WARREN, Boston M. & S. J. **194**:45, 1926.

A new interpretation is offered of the pathologic condition of the pancreas in diabetes mellitus. The long-continued action of an injurious agent (or possibly excessive functional activity) causes a gradual destruction of island, and at times of acinar cells. New cells are formed to take the place of those destroyed, only to be exposed to the injurious influence with consequent pathologic change. Their injury is followed by the production of more new cells. The rarity of

death from uncomplicated diabetes in cases of long duration is consistent with the conception of regeneration of the islands of Langerhans.

The first two years of the disease constitute the danger zone, during which period especial effort should be made to protect the patient against coma.

The disturbed carbohydrate metabolism giving rise to abnormal fat or protein metabolites may be a contributing cause of the high incidence of vascular disease in diabetic patients.

AUTHORS' SUMMARY.

THE EFFECT OF HIGH PROTEIN DIETS ON THE KIDNEYS OF RATS. H. JACKSON, JR., and M. D. RIGGS, *J. Biol. Chem.* **67**:101, 1926.

No recognizable nephritis could be produced in rats by the feeding of very high protein diets over a period of one third of the animal's life.

ARTHUR LOCKE.

LEUKEMIA, PSEUDOLEUKEMIA AND RELATED CONDITIONS IN THE SLYE STOCK OF MICE. JAMES P. SIMONDS, *J. Cancer Res.* **9**:329, 1925.

Among the 316 mice in the first 15,000 necropsies of the Slye stock studied because they showed enlargements of the lymph glands and spleen, there were 67 with leukemia, of which 28 were of the lymphatic and 39 of the myelogenous type; 111 pseudoleukemias, and 51 lymphosarcomas.

Typical instances of these conditions can be recognized without great difficulty. Leukemia and pseudoleukemia possess in common marked invasive power of the cells of the lymphoid tissues, the cells growing through the walls of veins and the capsules of lymph glands and infiltrating the surrounding tissues. In both there is widespread involvement of the lymph glands of the body with infiltration of one or more of the viscera without relation to the affected glands. They differ from each other in the number of nucleated cells in the blood. Lymphosarcoma is distinguished by its greater invasiveness and by being localized in one group of glands from which it may invade related organs. But generalized lymphosarcomatosis does occur in which the manner of spread is not readily apparent.

Borderline or transition cases are numerous. A generalized lymphosarcoma may closely resemble a pseudoleukemia; a subleukemic pseudoleukemia is not easily differentiated from a true leukemia; a leukosarcoma partakes of the characteristics of both leukemia and lymphosarcoma; in some cases of pseudoleukemia the lesion in one lymph gland or one group of glands may be so extremely invasive as to resemble a lymphosarcoma. An attempt has been made to establish criteria whereby these difficult cases may be classified correctly.

Lymphoid hyperplasia may be either local or generalized. This condition differs from the diseases mentioned above chiefly in the absence of the quality of invasiveness.

Anatomically and histologically, leukemia, pseudoleukemia and lymphosarcoma in these mice have distinctive features which indicate that they are probably fundamentally of the same nature and probably belong among the true neoplasms.

AUTHOR'S SUMMARY.

CALCIFIED RENAL CYST. THOMAS J. KIRWIN, *J. Urol.* **15**:273, 1926.

This is a discussion of the literature on solitary renal cysts, with report of a case with calcification of the wall.

SPONTANEOUS RUPTURE OF THE OESOPHAGUS. T. H. WILLIAMS and W. BOYD, Surg., Gynec. & Obst. 42:57 (Jan.) 1926.

A perforation of the esophagus just above the diaphragm was found in a man of alcoholic habits who died twenty hours after an acute onset of vomiting and excruciating pain in the chest. Dark fluid and food were present in the left pleural cavity. Sections taken through the lesion showed a chronic and subacute inflammatory process and numerous gram-positive bacilli and a few gram-positive diplococci. A similar inflammatory change with absence of the mucosa was noted in sections taken through the cardiac orifice. In experimental perforations of the esophagus in two dogs, no inflammatory change in the esophagus was found. The fluid found in the pleural cavities contained numerous bacilli and cocci. The pleura was intensely inflamed and covered by fibrinous exudate. In view of the intense and rapidly developing reaction in the pleural cavity, drainage should be instituted as early as possible. It is probable that some chronic inflammatory process precedes "spontaneous" rupture.

N. ENZER.

AMYOTROPHIC MENINGO-MYELITIS. J. P. MARTIN, Brain 48:153, 1925.

Histologic studies of the cords of syphilitic patients having atonic muscular atrophies revealed a chronic leptomeningitis over the entire cord. There was a severe granular ependymitis and toward the surfaces of the brain stem there was an intense glial reaction. A severe degeneration of the white matter around the surface of the cord was found, and less degeneration in the central white matter. Marked degeneration of the anterior horn cells and the cells of Clarke's column was present, which was almost complete in the cervical region. There was a moderate arteritis and perivascular lymphocytic infiltration. The entire picture was that of a syphilitic meningo-myelitis. The primary meningeal inflammation probably resulted in the cord lesions because of occlusion and stasis of the vessels and lymph channels. The clinical and pathologic observations were combined to set up this new entity of amyotrophic meningo-myelitis.

ROY GRINKER.

THE HISTOLOGY OF JUVENILE AMAUROTIC IDIOCY. GREENFIELD and HOLMES, Brain 48:182, 1925.

Two cases with gross atrophy of the cerebellum are described. Characteristic globoid distention of the cells with granular lipoid material was found throughout. The neurofibrils within the cells were well preserved although compressed to the side. Nissl bodies were absent or diminished. There was an overgrowth of glial fibers in the subpial layers. The perivascular spaces contained lipoid material. In the cerebellum the Purkinje cells were severely affected, and the molecular layer was almost completely degenerated. The perimacular portion of the retina was most involved, especially in the outer ganglion layer. Proliferation of pigment cells in the retina took place, and in areas these cells were degenerated. The outer ganglion layer was invaded by much sclerotic tissue and by granules of pigment. Pigment granules were also found between the rods and cones.

ROY GRINKER.

THE MECHANISMS OF SPEECH AND DEGLUTITION IN PROGRESSIVE BULBAR PALSY. M. CRITCHLEY and C. KUBIK, Brain 48:492, 1925.

In six cases of progressive bulbar palsy there was degeneration of the pyramidal tracts of the cord. The nucleus ambiguus was severely affected while

the dorsal vagal nucleus was spared. The paralyzed and wasted muscles contained a large amount of muscle tissue, and many of the fibers were only moderately affected. The atrophy was patchy, with varying intensity from moderate increase in the sarcolemma nuclei of apparently normal fibers to complete atrophy. The atrophy and clinical wasting were disproportionate owing to the loss of fat. The excessive loss of function was due to the involvement of the upper motor neuron. The tongue, laryngeal, pharyngeal and hyoid muscles were all affected. The atrophy proceeds with subdivision longitudinally of the muscle fibers, diminution in their size, increase in sarcolemma nuclei, and gradual replacement by connective tissue. No fatty infiltration was seen.

ROY GRINKER.

PLASMA LIPOID IN RENAL DISEASE. W. R. DANIELS, Brit. J. exper. Path. **6**:283, 1925.

The results of the examination of the plasma lipoids and plasma proteins in eighteen cases of renal disease are reported by Daniels. The plasma lipoids were increased in five of seven cases of chronic parenchymatous nephritis examined. In other forms of renal disorder examined, no similar increase of plasma lipoids was found. The average cholesterol and lecithin values were less than those found in normal persons. The average fatty acid value, on the other hand, slightly exceeded that found normally. No quantitative relationship appeared to exist between the plasma lipoids and the plasma proteins.

HYPERTROPHIC PNEUMONIC OSTEO-ARTHROPATHY IN A LIONESS. V. BAIL and C. LOMBARD, Bull. de l'Acad. de méd. **95**:16, 1926.

Pulmonary lesions and general changes had grown steadily worse since the 10 year old animal had last borne young. At necropsy all the bones appeared involved, especially those of the legs and pelvis. The lungs presented lesions of chronic tuberculosis with bronchiectasis; there was also fatty degeneration of the liver.

LEPROSY AS CAUSE OF DEATH. E. V. PINEDA, J. Philippine Islands M. A. **5**:360, 1925.

In comparatively few cases does leprosy cause death directly either from acute leprous febrile reactions or of leprous cachexia later. Death may result also from laryngeal obstruction by leprous granulation tissue.

ACUTE ORCHITIS AND EARLY SPERMATOGENESIS. H. KUNTZEN, Virchows Arch. f. path. Anat. **258**:108, 1925.

Kuntzen reports the incidental finding of an acute phlegmonous orchitis in a 9 months old boy who died of acute infection. The testes appeared normal grossly. Microscopically they were acutely inflamed, and the tubular epithelium was in a condition of active spermatogenesis. Although the relationship is not apparent, the author opens his article with a brief discussion of precocious puberty. Attempts to bring about active spermatogenesis in young guinea-pigs as the result of experimentally produced orchitis failed, except in the case of one animal in which intratesticular injection of a suspension of cholesterol was associated with a moderate degree of activity in the cells of the seminal tubules.

O. T. SCHULTZ.

CONGENITAL ECCHONDROSIS. F. SPEISER, *Virchows Arch. f. path. Anat.* **258**:126, 1925.

Speiser describes a case of generalized ecchondrosis in a boy who died at the age of 4½ years. The periosteum, the growth cartilages of the epiphyses of the long bones, the cartilage between the osteogenic centers of the bones and the cartilages of the synchondroses all took part in the proliferative process. The latter is considered a developmental anomaly which has its origin in the fourth to eighth fetal month.

O. T. SCHULTZ.

PROTEINOGENOUS PIGMENTATION OF BLOOD VESSELS. KLARA NOODT, *Virchows Arch. f. path. Anat.* **258**:156, 1925.

Noodt made a systematic study of the occurrence of brown, iron-free, supposedly proteinogenous pigment in the walls of the blood vessels of the organs of 401 persons more than 40 years old at the time of death. In fifty of these, pigment was present. The pigment was iron-free; it was bleached by hydrogen peroxide; it reduced silver nitrate, it was not colored by sudan III; but it did give a Smith-Dietrich reaction for phosphatids. The pigment is not lipoidal, however, as the phosphatid reaction was not given after treatment of the tissue with alcohol, although the original brown color remained. The pigment is, therefore, believed to be an endogenous proteinogenous substance which is loosely combined with the phosphatid. The pigment is usually situated in both arteries and veins; never in the latter alone. It occurred most often in the vessels of the pancreas, and in decreasing order of frequency in the kidney, liver, spleen, prostate, thyroid, testis, seminal vesicle and lung. It was localized usually in both connective tissue and muscle cells of the adventitia. In one case of hemochromatosis a similar proteinogenous pigment was present in the blood vessels of all the organs except the brain, being greater in amount in smooth muscle cells than in connective tissue elements.

O. T. SCHULTZ.

LIPOID DEPOSITION IN THROMBI. W. D. ZINSERLING, *Virchows Arch. f. path. Anat.* **258**:165, 1925.

As a contribution to the still open controversy as to whether lipid infiltration (Aschoff, Anitschkow) or functional and mechanical degenerative change (Thoma) is the primary factor in atherosclerosis, Zinserling studied the process of lipid infiltration of organized and of fresh unorganized thrombi of the heart and large vessels. He concludes that the lipid infiltration of unorganized thrombi is identical with that which occurs in the early stage of atherosclerosis, whereas the infiltration which occurs in organized thrombi is similar to that of the later stages of atherosclerosis. Since functional and mechanical factors are not active in thrombi, the author accepts the similarity of the infiltrative process of the latter with that of the artery wall as evidence that atherosclerosis is primarily an infiltrative process.

O. T. SCHULTZ.

CONGENITAL STENOSIS AND ATRESIA OF THE EXTERNAL AUDITORY CANAL. G. POLITZER and E. G. MAYER, *Virchows Arch. f. path. Anat.* **258**:206, 1925.

In eight cases studied there were found anomalies of the tympanic portion of the petrous bone, which was hypoplastic, hyperplastic or aplastic. The time of origin of the developmental anomaly is placed in the second to third fetal month. The described anomaly is much more frequent in females than in

males. Of the reported cases of atresia, the condition was bilateral in 28.5 per cent, left sided in 21 per cent and right sided in 50.5 per cent.

O. T. SCHULTZ.

LIPOID INFILTRATION OF SPLEEN IN DIABETIC LIPEMIA. N. SCHÖNDORFF, Virchows Arch. f. path. Anat. **258**:246, 1925.

Schöndorff reports a case of splenomegaly in a patient with marked lipemia who died in diabetic coma. Six previously reported similar cases are discussed. In Schöndorff's case the enlargement of the spleen, which weighed 450 Gm., was due to the presence of large cells which lay between the sinuses. From his microchemical studies, Schöndorff concluded that the material present in the large reticulo-endothelial cells is a phosphatid mixed with cholesterol esters. The condition is held to be the result of phagocytosis by reticulum cells of fatty and lipoid substances from the blood and tissue fluids. The infiltrating material is not chemically identical in the reported cases. It may be neutral fats, phosphatids or cholesterol esters, or a mixture of these substances. Because of the rapidly fatal course of the severe diabetic lipemias, the condition described usually remains limited to the spleen. The lipoid infiltration may be associated with a moderate degree of hemosiderosis of the enlarged cells. The author terms the condition an acute internal form of xanthomatosis, and believes that the lipoids are taken up directly from the circulating blood and tissue fluids, whereas in xanthomatosis they are taken up from stagnating fluids in the lymph and tissue spaces. Although the spleen in the condition described bears on cursory examination a striking resemblance to Gaucher's disease, the two processes are quite distinct, both as to the chemical nature of the substances involved and as to localization of the enlarged cells.

O. T. SCHULTZ.

AMYLOIDOSIS ASSOCIATED WITH HYPERNEPHROMA OF THE KIDNEY. W. SCHÄFER, Virchows Arch. f. path. Anat. **258**:268, 1925.

Schäfer adds one case to eleven previously reported, in which hypernephroma was associated with amyloidosis.

O. T. SCHULTZ.

XANTHOMA CELLS IN ORGANIZED THROMBI. W. PAGEL, Virchows Arch. f. path. Anat. **258**:414, 1925.

Pagel describes the occurrence of numerous xanthoma foam cells in the organized thrombi which filled the obliterated branches of the pulmonary artery in a case of tuberculosis of the lung. The process is not infrequent in the obliterated pulmonary vessels of chronic abscesses and tuberculosis of the lungs and is believed to bear a relation to fats and lipoids liberated locally in these conditions.

O. T. SCHULTZ.

HETEROTOPIC BONE FORMATION IN OVARIAN TRANSPLANTS. H. E. V. VOSS, Virchows Arch. f. path. Anat. **258**:419, 1925.

The formation of true bone is described by Voss in the transplanted ovaries of guinea-pigs. The process is one of indirect metaplasia, the proliferating connective tissue becoming dedifferentiated and transformed into a fibrillated osteoid tissue which becomes calcified. The resulting bone is membranous, although osteoblasts may arise and may form a small amount of compact bone. Marrow spaces may be formed; these contain embryonic marrow in which megakaryocytes may be present.

O. T. SCHULTZ.

HYPOPHYSIAL CHANGES IN DIABETES. J. SAKAKIBARA, *Virchows Arch. f. path. Anat.* **258**:430, 1925.

Sakakibara examined microscopically the hypophysis in ten fatal cases of diabetes, comparing his observations with those in forty cases in which death was due to other causes. He disagrees with Kraus, Verron, Schwab and others, who claim that the anterior lobe of the hypophysis becomes decreased in size in diabetes by the disappearance of the eosinophilous cells. He concludes that specific changes do not occur in the hypophysis in diabetes.

O. T. SCHULTZ.

PERIARTERITIS NODOSA WITH SYMPTOMS OF GALLBLADDER AND KIDNEY INVOLVEMENT. G. B. GRUBER, *Virchows Arch. f. path. Anat.* **258**:441, 1925.

To his numerous previous publications on periarteritis nodosa, Gruber adds a detailed account of a case in which gallbladder symptoms had led to cholecystectomy. Microscopic examination of the removed organ established the diagnosis of periarteritis nodosa. Symptoms of renal involvement made their appearance and death occurred in uremia, the duration of the illness from the first onset of muscular pain being eight months. Postmortem examination of the kidneys showed these also to be the seat of active periarteritis nodosa. Further examination showed evidences of healed periarteritis nodosa of the myocardium, kidneys, mesentery, periaortic tissue, vas, epididymis and voluntary musculature. The case report is followed by a careful discussion of the rarity of the involvement of the gallbladder in periarteritis in 110 reported cases, of the great frequency of renal involvement and of Gruber's conception of the nature of the disease. He concludes that the clinical syndrome is not characteristic, but is dependent on areas of active arterial involvement, and that the disease is not due to any single specific infectious agent. He defines periarteritis nodosa as a condition of local allergy which manifests itself in those portions of the walls of arteries which have been sensitized by previous localization of infectious agents or their products.

O. T. SCHULTZ.

EPITHELIAL HETEROTOPIA OF MECKEL'S DIVERTICULUM. G. SCHAEZT, *Beitr. z. path. Anat. u. z. allg. Pathol.* **74**:115, 1925.

In an article of 179 pages, Schaetz describes in detail the results of a microscopic investigation of thirty examples of Meckel's diverticulum, the object of the study being the determination of the frequency and type of epithelial heterotopia encountered. The normal lining of the diverticulum is held to be that of the ileum. Epithelium like that normally occurring in the jejunum, duodenum, stomach or pancreas is, therefore, considered heterotopic. Three of the thirty diverticula examined contained jejunal or duodenal mucosa. In five cases islands of gastric mucosa were present. Three cases contained islands of pancreatic tissue; the latter was well differentiated, and consisted of acini, ducts and islets. One diverticulum contained carcinoid tissue; the origin of the latter accepted by Schaetz is from Krompecher's basal epithelial cells as the result of embryonic maldevelopment. In one specimen there were found glandlike structures whose nature could not be determined; these were believed to have arisen from misplaced embryonic coelomic epithelium. The heterotopic epithelial elements were sometimes found combined with each other, and whether occurring alone or combined, they were usually situated at the tip of the diverticulum. The heterotopias described were not believed to be the result of

variations in differentiation of the original epithelium of the omphalomesenteric duct, but of auto-implantation of embryonic cells derived from different portions of the fetal intestinal tract. The portion of the duct represented by the tip of the diverticulum is narrow and favors lodgment and implantation of transported cells.

O. T. SCHULTZ.

EXPERIMENTAL AMYLOIDOSIS. S. UCHINO, Beitr. z. path. Anat. u. z. allg. Pathol. **74**:405, 1925.

As the result of experimental investigations in mice, Uchino concludes that the amyloidosis which follows repeated subcutaneous injections of nutrose is not due primarily to this substance, but that bacterial products are an important factor. The amyloid deposition occurs in the lymphoid tissues of the spleen and lymph nodes. The earliest change noted was death of cells of the germinal centers of the follicles, following which there occurred regenerative and hyperplastic changes in the germinal centers, which, in agreement with Flemming, are considered the sites of formation of lymphocytes. The amyloid deposition occurs first in the peripheral zones of the follicles.

O. T. SCHULTZ.

Pathologic Chemistry

THE CHEMICAL INVESTIGATIONS OF CORPUS LUTEUM. IV. THE ACETONE-INSOLUBLE FAT. G. F. CARTLAND and M. C. HART, J. Biol. Chem. **66**:619, 1925.

The fatty acid mixture from corpus luteum contains approximately 25 per cent palmitic, 11.2 per cent stearic, 1.6 per cent $C_{18}H_{34}O_2$, 32.8 per cent oleic, 16.6 per cent linolic, 8 per cent arachidonic and 4.8 per cent of $C_{20}H_{38}O_2$ acid.

V. THE LIPOIDS OF THE ACETONE EXTRACT. M. C. HART and F. W. HEYL, *ibid.*, p. 639.

There are present: cholesterol, cholesteryl palmitate, potassium stearate, leucine, isoleucine, valine, tristearin, a lecithin, and possibly sphingomyelin.

ARTHUR LOCKE.

THE FORMATION OF LACTIC ACID BY DEPANCREATIZED DOGS. C. J. WEBER, A. P. BRIGGS and E. A. DOISY, J. Biol. Chem. **66**:653, 1926.

Depancreatized dogs retain the capacity of forming lactic acid during strychnine convulsions or running. They exhibit a remarkable tenacity for the lactic acid precursor substance of muscle. The concentration of this substance falls rapidly to low values on the administration of epinephrine.

ARTHUR LOCKE.

THE SITE OF AMMONIA FORMATION AND THE PROMINENT RÔLE OF VOMITING IN AMMONIA ELIMINATION. S. BLISS, J. Biol. Chem. **67**:109, 1926.

Ammonia formation is a generalized tissue phenomenon, although glandular tissues produce the most. The blood ammonia values are increased in nephritis.

ARTHUR LOCKE.

TOTAL ACID-BASE EQUILIBRIUM OF PLASMA IN HEALTH AND DISEASE. I. THE CONCENTRATION OF ACIDS AND BASES IN NORMAL PLASMA. J. P. PETERS, H. A. BULGER, A. J. EISENMANN and C. LEE, *J. Biol. Chem.* **67**:141, 1926.

Normal serum contains 147-161 millimols of monovalent base, and 138-148 millimols of this base are combined with the four acids: protein, bicarbonate, chloride and phosphate. The limits are extended, for hospital patients, to 145-167 for total base and 135-155 for total acid. The content of organic acid does not exceed 20 millimols in persons in whom there is no disturbance of electrolyte equilibrium. Protein, bicarbonate, and chloride tend to reciprocate in their changes and to aid one another in maintaining the total acid and total base at a constant level.

II. THE EFFECT OF CO₂ TENSION ON THE CONCENTRATION OF THE ACIDS OF THE PLASMA OF OXYGENATED BLOOD. A. J. EISENMANN, H. A. BULGER and J. P. PETERS, *ibid.* p. 159.

When the carbon dioxide tension of the blood is increased from 30 to 60 mm. at 38 C., the blood cells swell slightly, diminishing the volume of the plasma and consequently augmenting the concentration and base-combining power of protein and, to a lesser extent, of phosphate. This is a little more than offset by the diminution of the acid values of protein brought about by reduction of *p_H*. The loss of water from plasma to cells results in a concentration of base that neutralizes the excess acid because base does not traverse the cell membrane.

III. THE DIFFERENCES BETWEEN ARTERIAL AND VENOUS BLOOD. J. P. PETERS, H. A. BULGER and A. J. EISENMANN, *ibid.* p. 165.

Arterial and venous blood differ in their electrolyte equilibria. They contain different amounts of water and chloride and have different carbon dioxide absorption curves.

IV. THE EFFECTS OF STASIS, EXERCISE, HYPERPNEA, AND ANOXEMIA; AND THE CAUSES OF TETANY. J. P. PETERS, H. A. BULGER, A. J. EISENMANN and C. LEE, *ibid.*, p. 175.

A disturbance of electrolyte equilibrium evokes a train of reactions and changes in all the other electrolytes. The response is not directed toward the maintenance of the concentration of any single constituent or group of constituents except as they may best serve to restore equilibrium and maintain the functional automatism of the whole organism. Prolonged venous obstruction—in which the escape of carbon dioxide through the lungs is prevented—leads to a transfer of water from the blood to the tissues and a concentration of proteins. The plasma chloride diminishes, yielding its base to protein and carbonic acid. Symptoms of tetany follow rapid overventilation; the carbon dioxide combining capacity and the total base remain unchanged, but the total carbon dioxide of the serum and the chlorides are diminished, and ketone acids are increased in amount. In extreme anoxemia the organic acid content rises and is neutralized by base derived from the tissues. Chloride and bicarbonate change in reciprocal directions. The loss of chloride, as by vomiting, appears to diminish the ability of the organism to prevent tetany by readjusting the acid-base balance after loss of carbonic acid.

V. MISCELLANEOUS PATHOLOGIC CONDITIONS, *ibid.*, p. 219.

The bicarbonate content is generally a little below the normal level following infections, probably due to the reaction of temperature which reduces the carbon dioxide combining capacity of the blood. The impairment of the respiratory mechanism in pneumonia causes the carbon dioxide to be maintained at a relatively high tension to facilitate its escape in the lungs, and the increased requirement of blood base is compensated by a loss of chloride from the blood.

ARTHUR LOCKE.

A NEW SULFUR-CONTAINING COMPOUND (THIASINE) IN THE BLOOD. S. R. BENEDICT, E. B. NEWTON and J. A. BEHRE, *J. Biol. Chem.* **67**:267, 1926.

Thiasine melts sharply at 262-263 degrees. It has the approximate constitution $C_{12}H_{12}N_2O_2S$, and molecular weight 300. It reduces the complex tungstic acid reagents commonly used for the determination of uric acid and gives a color approximately one-fourteenth as great as that given by an equivalent quantity of uric acid. The thiasine content of human blood averages about 14 to 15 mg. per hundred cubic centimeters. Values from 20 to 27 mg. per hundred cubic centimeters of blood are obtained from diabetic persons. The values are normal or low in nephritis.

ARTHUR LOCKE.

CHEMICAL INVESTIGATIONS ON NEOARSPHENAMINE. I. METHODS OF ANALYSIS. L. FREEDMAN, *J. Lab. & Clin. Med.* **11**:528, 1926.

A reversible reaction takes place when arseno compounds are titrated with iodine in the presence of a mineral acid, less iodine being required than is theoretically necessary. The extent of this reversible reaction is directly proportional to the increase in acidity of the titrated solution. Organic acids also have a tendency to promote this reversible reaction, but to a much smaller degree than mineral acids. The combined formaldehyde sulfoxylate group in neo-arsphenamine is oxidized by iodine in neutral solution to the corresponding formaldehyde bisulphite group, requiring 2 atoms of iodine. In the presence of even dilute solutions of hydrochloric acid, the combined formaldehyde sulfoxylate group undergoes a certain amount of hydrolysis, thus requiring more than 2 atoms of iodine for this group. For complete oxidation of this group, 4 atoms of iodine or 2 of oxygen are required. Strong solutions of hydrochloric acid (10 per cent or over) will completely hydrolyze neo-arsphenamine into arsphenamine and the decomposition products of formaldehyde sulfoxylate. Arsphenamine hydrochloride has actually been isolated from this reaction.

S. A. LEVINSON.

VARIATIONS IN THE BLOOD-SUGAR CONTENT FOLLOWING THE ADMINISTRATION OF INSULIN. H. J. JOHN, *J. Lab. & Clin. Med.* **11**:548, 1926.

The amount of insulin administered intravenously appears to bear no regular relation to the fall of blood sugar. While the administration of insulin usually produces a decrease in the blood sugar, in some instances it is followed by an increase which may or may not be related to postprandial hyperglycemia. In general, whatever the primary effect of insulin, repeated doses result in a decrease in the blood sugar; this apparently cumulative effect, however, is independent of the size of the doses. The level of blood sugar per se is not a criterion of the probability that a reaction will follow the administration of insulin. Thus a large dose of insulin may be given in the presence of hypo-

glycemia without any resultant reactions; and in another case a reaction may occur in the presence of a marked hyperglycemia.

S. A. LEVINSON.

ON ANAPHYLAXIS WITH HEATED SERUM. J. FURTH, *J. Immunol.* **11**:215, 1926.

Anaphylactic shock may be produced by horse serum heated to 100 C. in guinea-pigs sensitized by the same antigen. Uterine strips of guinea-pigs sensitized to heated horse serum react regularly to an otherwise harmless dose of the same antigen.

S. A. LEVINSON.

ECLAMPSIA, UNUSUAL NONPROTEIN NITROGEN IN BLOOD. R. D. MUSSEY, *Am. J. Obst. & Gynec.* **10**:826 (Dec.) 1925.

The notable feature of the case reported was the unusually high non-protein nitrogen retention observed in the blood for some time after delivery of a still-born fetus. On the third day, the urea was 164 mg. and uric acid was 18.3 mg. per hundred cubic centimeters of blood. On the fifth day the urea was 221 mg. and creatinin and uric acid each 14.5 mg. From then on the nonprotein nitrogen decreased; on the seventeenth day there was 43 mg. urea, 3.5 mg. creatinin, and 3.1 mg. uric acid per hundred cubic centimeters of blood. On the following day the phenolsulphonphthalein functional test was 30 per cent. Two months later renal function was normal and the nonprotein nitrogen of the blood was within normal limits.

A. J. KOBAK.

THE PRESENCE OF AN OXYTOXIC SUBSTANCE (POSTERIOR HYPOPHYSIS EXTRACT) IN CEREBROSPINAL FLUID. S. SHAPIRO, *Arch. Neurol. & Psychiat.* **15**:331, 1926.

In using cerebrospinal fluid from various neurologic patients in normal concentrations on isolated virgin guinea-pig's uterus there resulted no contraction. A prolongation of the relaxation period took place and the succeeding contraction was diminished in amplitude and duration. Applying the spinal fluid during a contraction shortened the contraction and hastened relaxation. Three cubic centimeters of fluid could counteract the action of pituitary extract of 1:10,000 to 1:100,000 varying with the preparation.

ROY GRINKER.

INTESTINAL CHEMISTRY. III. SALIVARY DIGESTION IN THE HUMAN STOMACH AND INTESTINES. O. BERGEIM, *Arch. Int. Med.* **37**:110, 1926.

The extent of salivary digestion of the starch of a test meal may be determined in the course of a gastric analysis, using the retention stomach tube. Bread or other foods containing a known amount of iron oxide may be used in studies of gastro-intestinal digestion and absorption, iron determinations serving as a guide in interpretation of the results. Studies of salivary digestion in the stomachs of normal men showed on the average 75 per cent of the starch of mashed potatoes and 59 per cent of the starch of bread to be converted to maltose, an additional percentage being changed to dextrins. This considerable degree of starch conversion was generally brought about within from fifteen to thirty minutes after the meal was finished, active amylase disappearing and free hydrochloric acid appearing simultaneously. Salivary amylase is inactivated by low concentrations of free hydrochloric acid even in the presence of starch and its digestion products, and does not again become active when the acidity is neutralized. Neither is it possible to reactivate, by the addition of

small amounts of active amylase, saliva that has been inactivated by acid or by boiling. To function in the intestine, saliva must escape the action of acid gastric juice.

S. A. LEVINSON.

PENTOSURIA, FIVE CASES IN ONE FAMILY. HAROLD W. JONES and C. W. NESSLER, *Ann. Clin. Med.* 4:505, 1925.

There is some evidence that pentosuria may depend on oxidation of inactive galactose. Pentose does not ferment, gives a green precipitate and color with Bial's reagent and a characteristic crystal with the phenylhydrazine test; the crystals have a melting point of 156 to 160 C. Five cases are reported of the "essential" type in one family—Jewish—in which race the condition seems to be most prevalent.

SIGNIFICANCE OF GUANIDINES IN ANIMAL BODY. N. PATON, Glasgow M. J. 22:297, 1925.

It seems to Paton that the free guanidines act in determining muscle tone, possibly by their influences on the endings of the sympathetic nerves; that they are produced in the liver from the cholin of lecithin, and that their formation may be controlled by the condition of the muscles, as the formation of sugar is controlled; that their action on the muscles is governed by the internal secretion of the parathyroids, which regulates their change into the inert creatin, and that probably the outflow of the secretion from the parathyroids is called forth by the condition of the muscles.

THE INTRACELLULAR FERMENTS OF THE LIVER, ESPECIALLY IN PHOSPHORUS POISONING. STAEMMLER, *Klin. Wchnschr.* 5:134, 1926.

The primary injury in phosphorus poisoning of the liver is on the synthetic action of the diastases, which leads to a disappearance of liver glycogen and an increased deposition of fat.

ARTHUR LOCKE.

A CHARACTERISTIC BLOOD-SUGAR REACTION IN ULCUS VENTRICULI. W. SCHARPFF, *Klin. Wchnschr.* 5:138, 1926.

There is a considerable increase in the blood-sugar values after a feeding of 80 Gm. of levulose in 300 cc. of fluid to persons with gastric or duodenal ulcers. This increase is weak or entirely lacking in persons with gallbladder affections.

ARTHUR LOCKE.

THE RELATIONS OF THE BLOOD-PROTEIN SUBSTANCES AS A MIRROR OF DEFINITE PATHOLOGIC PROCESSES IN THE HUMAN ORGANISM. THE LABILE GLOBULIN SERUM PROTEIN QUOTIENT. G. LEENDERTZ, *Klin. Wchnschr.* 5:175, 1926.

A method is given for the determination of the "labile globulin" content of serum. The rate of sedimentation of the erythrocytes from blood is a function of the quotient of this "labile globulin" content by the total protein content of the serum.

ARTHUR LOCKE.

A BLOOD URICO-OXIDASE AND THE TRUE VALUE OF THE BLOOD URIC ACID. FLATOW, *München. med. Wchnschr.* 73:12, 1926.

The uric acid content of the blood is much higher than would appear from present methods of analysis. A urico-oxidase arising from the formed con-

stituents of the blood quickly destroys 90 per cent of the uric acid normally present. The oxidase is partly carried into the deproteinized filtrate, is active in weakly acid and alkaline solutions, and is heat stable. It decomposes pure uric acid when the latter is added to the filtrate. There are only slight differences between the blood urico-oxidases of different animal species.

ARTHUR LOCKE.

THE PRESENCE OF IODINE IN HUMAN AND ANIMAL ORGANISMS. E. MAURER and St. DIEZ, München. med. Wchnschr. **73**:17, 1926.

There is a relation between the iodine deficiency and the swelling of the thyroid which occurs during menstruation and pregnancy. The iodine content of the venous blood is approximately 110 per cent above the normal level on the first day of menstruation. There is no marked increase during pregnancy. Breast milk, on the first day of lactation, has a very high iodine content, which later gradually decreases to the normal level.

ARTHUR LOCKE.

REVERSION OF HEMOLYSIS. W. STARLINGER, Deutsche med. Wchnschr. **52**:25, 1926.

In the same blood, after laking with water, about the same quantity of hemoglobin as escapes is bound again by the stroma on addition of salt. In pernicious anemia reversible hemolysis is marked. Blood transfusion and protein injections affect the amount of reversion.

POTASSIUM-CALCIUM RATIO IN BLOOD. E. KYLIN and G. MYHRMAN, Deutsches Arch. f. klin. Med. **149**:354, 1925.

Epinephrine was injected into 119 patients after determining the potassium and calcium content of the serum. The lower the potassium-calcium ratio, the stronger, generally speaking, was the rise in blood pressure (sympathicotonia). The higher the ratio, the more prominent was the lowering of the blood pressure (vagotonia). The second group occurs with asthma, essential hypertension and vagotonic neuroses. Diabetes in the young belongs to the first group. The calcium content varied in healthy persons between 10.6 and 12 mg. per hundred cubic centimeters; in pathologic conditions between 9.1 and 12.9. The potassium content varied in health between 18 and 23 mg.; in patients between 14.3 and 38.3. The potassium-calcium ratio was in health 1.70 to 2.15; in disease 1.35 to 3.48. The highest figures were obtained in a case of grave insufficiency of the kidneys.

ORIGIN OF GALLSTONES. R. BRÜHL, Beitr. z. path. Anat. u. z. allg. Pathol. **74**:294, 1925.

Brühl concludes that every gallstone is formed about a center of inert material as the result of alterations in the colloidal equilibrium of the bile. Calculi, which have a radial or radial concentric structure, and which are termed spheroliths, are formed as the result of emulsification of cholesterol. Stones composed of concentric layers of bile pigment, calcium and protein are formed by a primary precipitation of protein which becomes secondarily incrustated with bile pigment and calcium. Calculi grow by apposition and by adsorption. Crystallization of amorphous cholesterol may lead to changes in the structure of gallstones. A secondary cholesterolization of already formed stones, as postulated by Naunyn, is not believed to occur.

O. T. SCHULTZ.

Microbiology and Parasitology

CREEPING ERUPTION. J. L. KIRBY-SMITH, W. E. DOVE and G. F. WHITE, Arch. Dermat. & Syph. **13**:137, 1926.

A disease of the skin characterized by a creeping eruption is described from Jacksonville, Fla., as due to the larvae of a nematode named *Agamonematodum migrans*.

CUTANEOUS REACTION IN LEISHMANIASIS. JOAO MONTENEGRO (SÃO PAULO, BRAZIL), Arch. Dermat. & Syph. **13**:187, 1926.

Intradermal injections of an alkaline extract of *Leishmania* were given to thirty-seven patients with leishmaniasis, and positive reactions were obtained in thirty-two of them, or 86.5 per cent. Injections with the same extract were also given to thirty-six persons free from leishmaniasis. Of these, thirty-three developed negative reactions, and three showed a certain reaction definitely distinct from the specific reactions obtained with the patients who had leishmaniasis. It was much less intense. The cutaneous reaction of leishmaniasis is specific, and for this reason when typically positive is of itself sufficient to confirm the diagnosis if the patient has not had leishmaniasis before.

AUTHOR'S SUMMARY.

BACILLUS BRONCHISEPTICUS INFECTION IN A CHILD WITH SYMPTOMS OF PERTUSSIS. J. HOWARD BROWN, Bull. Johns Hopkins Hosp. **38**:147, 1926.

The close association of children with pet animals and the wide prevalence of *B. bronchisepticus* infection among these animals would indicate that human infection with this organism may be more common than has been recognized. It is not known whether the infection is readily transmitted from one child to another, but an interesting public health and epidemiologic problem is involved. It may be that in many supposed cases of pertussis the patients are needlessly quarantined, and it may be that if cases of *B. bronchisepticus* infection were correctly diagnosed there would be fewer cases of pertussis without a history of exposure to other cases.

AUTHOR'S SUMMARY.

CARBON DIOXIDE AS A FACTOR IN THE GROWTH OF THE TUBERCLE BACILLUS AND OF OTHER ACIDFAST ORGANISMS. GEORGE E. ROCKWELL and JOHN H. HIGHBERGER, J. Infect. Dis. **38**:92, 1926.

It is shown that the inhibition of growth of a saprophytic tubercle bacillus, two strains of virulent tubercle bacilli and two other acid-fast organisms, when incubated over alkalis in closed spaces, cannot be explained as being due to dehydration of the nutrient medium, since growth occurs over other equally or more efficient dehydrating agents which are not carbon dioxide absorbents, such as sulphuric acid, calcium chloride and glycerol. The only explanation which can account for this phenomenon is that carbon dioxide is, in some way, a vital factor in growth.

AUTHORS' SUMMARY.

VIABILITY AND TOXICOGENIC POWER OF SMALL NUMBERS OF SPORES OF *CL. BOTULINUM* SUBJECTED TO DIFFERENT TEMPERATURES. WILLIAM A. STARIN, J. Infect. Dis. **38**:101, 1926.

The thermal death point of limited numbers of spores of *Cl. botulinum* inoculated into ordinary vegetables, such as peas, corn, string beans and spinach,

is much lower than when mass contamination occurs. In a series of 384 cultures, with an inoculum of 9 to 12 detoxified spores in each culture, no growths were obtained subsequent to heating the inoculated tube at 100 C. for ten minutes. Growths were uniformly obtained when similar cultures were heated at the lower temperature of 70 C. for the same length of time.

Within these limits of exposure temperatures, the thermal death point is independent of the incubation temperature, practically the same results being obtained when the inoculations were kept at room temperature, at 27 C., or at 37 C.

No significant differences were observed in the results that might be dependent on the different varieties of vegetables used, except in the case of the spinach, in which growths were less rapid even when its reaction had been adjusted to a p_H of 7.6. When the spinach in a natural state, with a p_H of 5.3, was inoculated, growths and toxin production were scanty even in the unheated cultures, and none appeared in these cultures when the spores had been heated at 70 C., or a higher temperature, for ten minutes.

AUTHOR'S SUMMARY.

RELATIONSHIP OF INCUBATION TEMPERATURE TO VIABILITY, RATE OF GROWTH AND TOXIN PRODUCTION OF *CL. BOTULINUM* IN DIFFERENT VEGETABLES.
WILLIAM T. STARIN, J. Infect. Dis. **38**:106, 1926.

Temperatures of 20 C. and 25 C. are equally suitable for the growth of *Cl. botulinum* and for the production of botulinus toxin in such vegetables as corn, string beans, peas and spinach. The rate of development is somewhat more rapid at 25 C. than at 20 C., although in each case the toxicity eventually reaches the same level.

A temperature of 10 to 12 C. is not suitable for growth of *Cl. botulinum* nor for the production of a potent toxin, even when incubation is extended to five months.

Death of the organism does not occur at any temperature used, even after three months' incubation. Even in those mediums in which no evidence of growth or toxin production could be detected, transplants to a suitable medium, such as beef heart, resulted in abundant growth of the organism with normal toxin production.

Disintegration of the medium parallels the production of toxin, although in some instances lethal doses of toxin may be present with practically no noticeable changes in the gross appearance or in the odor.

The four vegetables used ranked as follows in the rate of toxin production and in the quantity of toxin produced: corn, peas, string beans, spinach.

The high initial acidity of the beans and spinach may be the responsible factor for the slight growth and toxin production in these mediums.

AUTHOR'S SUMMARY.

PULMONARY INFECTIONS BY FRIEDLÄNDER'S BACILLUS. WILLIAM P. BELK, J. Infect. Dis. **38**:115, 1926.

Eighteen cases of infection of the lung by *B. mucosus* were studied, and a provisional report is made of a chronic pulmonary lesion caused by this organism. Six cases of lobar pneumonia due to *B. mucosus* are reported in detail, with references to thirty-eight cases in the literature.

AUTHOR'S SUMMARY.

THE GERMICIDAL PROPERTIES OF SOAP. JOHN E. WALKER, J. Infect. Dis. **38**:127, 1926.

The meningococcus is killed in two and one-half minutes by N/80 to N/640 solutions (0.4 to 0.04 per cent) of the soaps of the fatty acids ordinarily present in soap bases; 1 per cent phenol is required to kill under the same condition.

The gonococcus is killed in two and one-half minutes by N/640 to N/5,120 solutions (0.04 to 0.006 per cent) of the same soaps; 0.5 per cent phenol killed under the same condition.

Sodium resinate also possesses marked germicidal activity toward these two organisms.

The meningococcus, on being tested with four commercial soaps, showed approximately the same degree of susceptibility as would have been anticipated from the action of the chemically pure soaps.

The susceptibility of meningococci and gonococci is such that they (along with streptococci, pneumococci and diphtheria bacilli) will be readily killed by any ordinary soap used with a reasonable degree of care.

The dysentery bacilli and paratyphoid bacilli react to the different soaps in the same manner as previously shown for typhoid and colon bacilli, that is, they are killed by moderate concentrations of the soaps of the saturated acids, but are completely resistant to the soaps of the unsaturated acids at ordinary temperatures.

The most readily available commercial soap to be used against the typhoid bacilli, paratyphoid bacilli and dysentery bacilli is salt water soap prepared exclusively from coconut oil.

AUTHOR'S SUMMARY.

INFLUENCE OF SOME ANAEROBIC SPECIES ON TOXIN OF *CL. BOTULINUM* WITH SPECIAL REFERENCE TO *CL. SPOROGENES*. GAIL M. DACK, J. Infect. Dis. **38**:165, 1926.

The filtered toxin of *Cl. botulinum* added to beef heart medium is gradually destroyed by the growth of *Cl. sporogenes* in it.

The power to destroy botulinum toxin is also possessed by several other anaerobic species with proteolytic and nonproteolytic properties.

The destruction of the toxin is not due to a change in hydrogen ion concentration.

Cl. botulinum type A (M7a⁺) grew scantily in a filtrate of *Cl. sporogenes*. Growth was more vigorous in a filtrate which had been boiled but still was invisible macroscopically. Toxin was demonstrated in all the tubes but was stronger in the tubes containing the filtrate which had been heated.

Cl. botulinum type B (126.7) did not grow in the unheated sporogenes filtrate, nor did it produce toxin.

No reduction in potency of the toxin of *Cl. botulinum* type A (M7a⁺) was noted when an equal amount of sporogenes filtrate was added to it.

No visible growth (macroscopically) of *Cl. sporogenes* occurred in a filtrate of *Cl. botulinum* after seven days' incubation at 37 C.

AUTHOR'S SUMMARY.

BEHAVIOR OF BOTULINUM TOXIN IN ALIMENTARY TRACT OF RATS AND GUINEA-PIGS. GAIL M. DACK, J. Infect. Dis. **38**:174, 1926.

Botulinum toxin when mixed with stomach tissue and abdominal wall tissue from guinea-pigs, and mice in vitro and incubated at 35 C. for one hour was

not reduced in potency except in two cases in which stomachs of mice were used. The reduction, however, was slight in these cases.

Botulinum toxin was not completely destroyed in the stomachs and small intestines of rats and guinea-pigs receiving injections of the toxin directly into the stomach. Its presence was definitely demonstrated after twelve hours in guinea-pigs and after three hours in rats.

In two cases of seven toxin was demonstrated in the blood of guinea-pigs fed with botulinum toxin. No toxin was found in the blood of rats fed with large doses of botulinum toxin.

Toxin was found in the blood of rats and guinea-pigs three hours after intravenous and intramesenteric injections of the toxin.

AUTHOR'S SUMMARY.

STUDIES ON RESPIRATORY DISEASES. XXVII. ELECTROPHORETIC POTENTIAL, ACID AND SERUM AGGLUTINATION OF PNEUMOCOCCI. I. S. FALK and M. A. JACOBSON, *J. Infect. Dis.* **38**:184, 1926.

The authors have found that for pneumococci, as has already been found for other bacteria, with increasing acidity the potential difference (P. D.) between bacteria and menstruum declines from negative values to an iso-electric point, then to increasing positive values, and, near $P_h = 0$, to a second isopotential point.

The iso-electric points of the pneumococci of types, 1, 2, 2 and 4 and of variants (B and C) of type 1 (A) are near $P_h = 3$ and are not significantly type specific.

The P. D. for pneumococci is correlated with the inagglutinability by acid. In general, it is found that the higher the P. D. at $P_h = 6.5$, the lower the P_h necessary to cause spontaneous agglutination.

The P. D. values for the variant types can be changed relatively by washing the bacteria. An inversion of the relative potentials on variants A, B and C is accompanied by an inversion in their agglutinability by acid.

Type-specific, homologous and heterologous antipneumococcus serum reduces the negative P. D.; the greater effectiveness of the homologous serum in this regard parallels its greater effectiveness in agglutinating the bacteria.

The correlation between potential and inagglutinability is further evidenced by the inversion of the relative stability of suspensions (A, B, C) when tested with agglutinating serum after they have been washed sufficiently to invert the relative magnitudes of the potentials.

AUTHORS' SUMMARY.

STUDIES ON RESPIRATORY DISEASES. XXVIII. THE ELECTROPHORETIC POTENTIALS, THE DISSOLUTION AND THE SERUM AGGLUTINATION OF PNEUMOCOCCI IN THE PRESENCE OF SODIUM OLEATE. I. S. FALK and M. A. JACOBSON, *J. Infect. Dis.* **38**:188, 1926.

The finding that the variant strains of pneumococci (A, B and C) which show marked differences in virulence for mice are equally soluble in bile or oleate solution is contradictory to the usual statement that virulence and solubility are parallel characteristics.

Bile is practically without effect on electrophoretic potential.

Sodium oleate effects significant increases in the potentials on pneumococci. From this finding it was anticipated that oleate would increase the stability of pneumococcus suspensions and would reduce the titers for serum agglutinations. These anticipations were confirmed by experiment.

These results provide a further confirmation of the view that the agglutinability of pneumococci is correlated with the electrophoretic potential.

AUTHORS' SUMMARY.

EFFECT OF THYROIDECTOMY AND OF THYMECTOMY IN EXPERIMENTAL SYPHILIS OF THE RABBIT. LOUISE PEARCE AND CHESTER M. VAN ALLEN, J. Exper. Med. **43**:297, 1926.

Experiments are described in which the thyroid or thymus gland of rabbits was removed prior to inoculation of the animals with *Spirochaeta pallida*. The effect of these procedures is described from the standpoint of the manifestations of the disease. After complete thyroidectomy, the disease was considerably more severe than in the controls and markedly so in certain instances. Partial thyroidectomy, on the other hand, resulted in a milder disease than that of the controls. The effect of complete thymectomy was less pronounced than that of either complete or partial thyroidectomy, but, in general, the syphilis resembled that in partially thyroidectomized animals.

These effects are discussed in relation to the host's reaction and resistance to experimental syphilis, and the conclusion was reached that the integrity and balance of the glands of internal secretion play an important rôle in the mechanism of defense against this infection.

AUTHORS' SUMMARY.

VARIATIONS IN CARBON DIOXIDE REQUIREMENTS AMONG BOVINE STRAINS AND *BACILLUS ABORTUS*. THEOBALD SMITH, J. Exper. Med. **43**:317, 1926.

Strains of *Bacillus abortus* freshly isolated vary in their carbon dioxide requirements. The origin and sources of the strains growing with less dependence on carbon dioxide (or sealing) may be in vaccinal strains or possibly in continued existence in the udder. The importance of these possibilities makes it desirable that all strains isolated should be subjected to some such test as is outlined in these pages.

AUTHOR'S SUMMARY.

FURTHER DATA ON THE EFFECT OF VACCINATION AGAINST BOVINE INFECTIOUS ABORTION. THEOBALD SMITH and RALPH B. LITTLE, J. Exper. Med. **43**:327, 1926.

The partial protection afforded by four injections of a heated culture of *Bacillus abortus* of normal virulence during the first pregnancy is in part lost in the second. The superiority of a single injection of a living culture of relatively low virulence is evident in both pregnancies. In the experiment described, the protection was complete.

AUTHORS' SUMMARY.

A RAPID METHOD FOR THE ISOLATION OF *BACILLUS ABORTUS* FROM UTERINE EXUDATE AND DISEASED PLACENTA. JOHN B. NELSON, J. Exper. Med. **43**:331, 1926.

A rapid method is described for the isolation of *Bacillus abortus* from the peritoneal cavity of the guinea-pig following the injection of uterine exudate or placental tissue.

AUTHOR'S SUMMARY.

STUDIES ON THE BIOLOGY OF STREPTOCOCCUS. V. ANTIGENIC RELATIONSHIPS
BETWEEN STRAINS OF STREPTOCOCCUS FROM SCARLET FEVER AND ERYSIPELAS.
FRANKLIN A. STEVENS and A. R. DOCHEZ, J. Exper. Med. **43**:379, 1926.

Strains of hemolytic streptococci isolated from cases of erysipelas agglutinate in a high percentage of instances with erysipelas immune serums. When agglutination occurs with one serum, the strain usually agglutinates with all other erysipelas serums.

Erysipelas immune serums agglutinate strains from erysipelas in a higher percentage of instances than they agglutinate scarlatinal strains.

Strains from miscellaneous pyogenic infections may agglutinate in these serums, but the percentage of positive reactions is low and a strain usually agglutinates in but one or two of several serums.

Erysipelas strains which agglutinate in immune serums are not necessarily identical, although identical strains may occur. Similarly, identical strains may occur among scarlatinal strains agglutinated by scarlatinal immune serums.

Erysipelas strains form a closely related group of hemolytic streptococci. Scarlatinal strains form an equally compact group. The two groups are related antigenically but less closely related than the strains within the groups. These groups are related to pyogenic strains, but less closely than they are related to each other.

Erysipelas, scarlatinal or pyogenic strains which agglutinate in erysipelas or scarlatinal serums are capable of absorbing the agglutinin for all other strains except the homologous strain and strains identical with it. Strains identical with the homologous strain absorb the agglutinin completely.

Erysipelas or scarlatinal strains may absorb the common group agglutinin from their respective serums when they are incapable of agglutination in these serums.

The agglutinin is probably of complex or composite nature, with characteristic variations in the scarlet fever and erysipelas groups.

AUTHORS' SUMMARY.

STUDIES ON THE COMMON COLD. I. OBSERVATIONS OF THE NORMAL BACTERIAL
FLORA OF THE NOSE AND THROAT WITH VARIATIONS OCCURRING DURING COLDS.
G. S. SHIBLEY, F. M. HANGER and A. R. DOCHEZ, J. Exper. Med. **43**:415,
1926.

The normal bacterial flora of the nose and throat of thirteen individuals has been studied over periods ranging from five to nine months. Observations have been made of qualitative and quantitative changes in the flora occurring in the course of colds and of throat infections appearing in the group.

The normal basic nasal flora includes *Staphylococcus albus*, diphtheroids and for certain individuals *Staphylococcus aureus* and *citreus*. Occasional transient bacteria are gram-negative cocci and nonhemolytic streptococci.

The normal basic throat flora includes gram-negative cocci, nonhemolytic streptococci, and for certain individuals "large gram-positive cocci," *B. influenzae*, *Bacillus "X"* and diphtheroids. Transient organisms are *Staphylococcus albus*, hemolytic streptococci, *Staphylococcus aureus* and *citreus*, and pneumococci.

No bacteria were found in early cold cultures to which a causative rôle could be assigned. In the course of colds, the basic flora of the nose was often scanty in the early stages. The throat showed reduction of prominence

or alterations in predominance of the basic flora. Certain organisms were prominent in colds, usually as late or secondary invaders; these included *Staphylococcus aureus*, hemolytic streptococci and *B. influenzae*. There was a striking increase in the incidence of hemolytic streptococci in throat infections.

AUTHORS' SUMMARY.

STUDIES ON BACTERIAL (INFECTIVE) ENDOCARDITIS. WILLIAM S. THAYER, Johns Hopkins Hosp. Rep. 22:1, 1925.

In a monographic clinical and anatomic study of 198 instances of bacterial endocarditis, the concluding observations are:

"Various recognized infectious agents, among which Streptococci, *Staphylococcus aureus*, *Pneumococcus*, *Gonococcus* and the Influenza group are the commonest examples, give rise more or less frequently, to focal endocardial disease, verrucous, vegetative or ulcerative, valvular or mural endocarditis, associated sometimes with acute, often suppurative pericarditis, and focal, often suppurative myocarditis. The endocardial lesions are, as a rule, the most important.

"Bacterial disease of the heart ('malignant' or 'infective' endocarditis) may be divided into two main forms: 1. In the first, the lesions appear commonly as complications or sequels of some focal inflammatory process with an accompanying septicaemia which is usually rapidly fatal. Under such circumstances the existence of cardiac disease is generally masked by the symptoms of the acute infection of which it is a complication. In peracute cases the lesions are verrucous, scarcely larger than those of rheumatic heart disease. In those with a course of several weeks the changes are usually vegetative or ulcerative. In most acute septicaemias the cardiac disease is clinically subsidiary to its mother infection—a mere incident in an acute septicaemia or pyaemia.

"2. In other instances, especially in infections with attenuated streptococci, notably *Streptococcus viridans*, and with *B. influenzae*, the endocardial focus is truly the main seat of the disease. The course of the malady is slow, subacute or chronic, lasting over weeks and months. The onset is insidious; the portal of entry is obscure; and the areas involved are generally the seat of previous chronic rheumatic disease. The manifestations are rather those of subacute or chronic septicaemia to which later the characteristic embolic phenomena are added. Here the subacute endocarditis is in itself the essential pathologic entity.

"While rheumatic heart disease is a true pancarditis, these recognized bacterial affections of the heart may be and often are, essentially or purely, endo-, peri, or more rarely, myocardial. The infrequency of extensive myocardial change is striking.

"With recovery which apparently is not very frequent, there remain deformed, sclerotic or calcified valves, or perhaps, an adherent pericardium or myocardial scars. But recovery is apparently relatively unusual.

"Syphilis is an important cause of disease of the aorta and often affects the aortic valve with resultant aortic insufficiency and its consecutive changes. It is probably associated with grave myocardial disease more commonly than is generally appreciated.

"Rheumatic fever and chorea stand together as manifestations of that infection which is associated with those peculiar acute cardiac changes which we have come to class as 'rheumatic.' The so-called 'rheumatic' cardiac lesions affect the entire heart. They consist of the peri-vascular Aschoff bodies, the frequent sero-fibrinous pericarditis, the slowly developing and cicatrizing

valvulitis and verrucous endocarditis, notably of the mitral orifice. These processes terminate in the familiar picture of chronic valvular disease of the heart with disseminated peri-vascular fibrosis of the heart-muscle, and often with adherent pericardium.

"The acute infections, other than rheumatic fever and chorea and syphilis, appear to play a small part in the production of chronic valvular disease of the heart."

A CONTRIBUTION TO THE ETIOLOGY OF CALCAREOUS PYELONEPHRITIS. B. H. HAGER, J. Urol. **15**:133, 1926.

Salmonella ammoniae can invade the kidney pelvis and under favorable conditions produce a calcareous pyelonephritis.

The mechanism of the production of alkaline urine with a precipitation of the alkaline inorganic salts in the pelvis and calices of the kidney is similar to the production of encrusted cystitis with free floating bladder stones in the bladder by the activity of *Salmonella ammoniae*.

AUTHOR'S SUMMARY.

STUDIES IN MICROBIC HEREDITY. III. THE HEREDITARY ORIGIN OF GROUP AND SPECIFIC AGGLUTINOGENS AMONG THE COLON-ALKALIGENES ORGANISMS. R. R. MELLON and E. YOST, J. Immunol. **11**:139, 1926.

B. alkaligenes can grow in the human body as a large gram-positive diplococcus and propagate itself for years as such on artificial mediums. By mutation it will dissociate into a bacillary stage and into a streptothrix-like stage and into a stage of mixed morphology, all of which will breed to their own types. There is evidence that this mutation process involves a primitive sexual cycle (zygospore formation) which appears to exist for this organism and *B. coli*. The type of pleomorphism here shown is directly comparable to the pleomorphism of the fungi, and strengthens the belief that bacteria are not monomorphic but are fungi imperfecti. Serologic interrelations have been shown to exist between these stabilized stages (variants) in the life history of a single organism. Group and specific agglutinogens have been shown to exist among these stages as well as between them and *B. coli*. The demonstration of the genetic history of this organism has made possible the discovery of group agglutinins in a serum that would conventionally be regarded as having only the specific variety. The failure to recognize the group agglutinins by usual agglutination technic is referred, first, to the presence of an inhibitory factor probably common to all serums, and second, to its selective adsorption by the strain in question. An almost identical variant serologically was but slightly affected by the inhibitory substance. The results show clearly that serologic reciprocity does not of necessity imply identity in other respects.

S. A. LEVINSON.

STUDIES IN MICROBIC HEREDITY. IV. OBSERVATIONS ON GROUP AGGLUTININS IN SPECIFIC SERA WITH THE TECHNIC OF CATAPHORESIS. R. R. MELLON and E. GRENQUIST, J. Immunol. **11**:161, 1926.

The cataphoresis method as applied to certain anomalies of the agglutination reaction confirms and extends the work of R. R. Mellon which deals with the hereditary origin of group and specific agglutinogens. It indicates that group agglutinins may be present in so-called specific serums, but their presence may not always be detected by standard methods for this test. With the

strains in question, the authors obtained results by employing a sensitization temperature of 20 C. instead of 37 C., which in some cases was reinforced by extending the time of observation. An explanation for the observation may rest on the apparent fact that some strains appear to have greater avidity for a nonspecific serum inhibiting factor at 37 C. than for group agglutinin, but that at 20 C. this effect is somewhat compensated. With one of the strains studied (K 84) either the products of autolysis or an inhibitory medium substance prevented the decrease of the electrical charge that occurred after washing the strains. Strains that appear to absorb specific agglutinin strongly show a noteworthy decrease in potential in immune serum. Moreover, this lowered charge may be still further decreased by washing the excess of immune serum from the organisms. On the other hand, washing off the immune serum from a sensitized organism had an opposite effect on a feebly binding strain. This effect consisted in a return of the decreased charge to its original level, or even to higher levels than it possessed before its subjection to the action of immune serum.

S. A. LEVINSON.

TUBERCULOSIS OF THE PLEURA. W. S. MILLER, *Am. Rev. Tuberc.* **13**:1 (Jan.) 1926.

Tubercles may develop either in the submesothelial or aveolar layer of the pleura. Bacilli may reach either layer through blood or lymph vessels; or a tuberculous process may extend from the lung tissue into the alveolar layer. When a cavity is formed just beneath the pleura, the pleura does not, as a rule, take part in the tuberculous process. The collagenous and elastic fibers seem to be definitely resistant to the extension of a tuberculous process. When the entire thickness of the pleura becomes involved, adhesions are formed between the two pleural leaves.

MAX PINNER.

EXPERIMENTAL INTRATRACHEAL INFECTION WITH THE TUBERCLE BACILLUS. T. D. BECKWITH and R. J. MILLZNER, *Am. Rev. Tuberc.* **13**:62 (Jan.) 1926.

After the injection of tubercle bacilli into the wall of the trachea one finds the tracheobronchial lymph glands regularly involved; there are relatively few lesions in the lungs. Tubercle bacilli are regularly found in the cervical lymph nodes, frequently without the formation of pathologic changes, from fourteen to thirty-two days after the infection. The authors believe that the pulmonary infection in these animals resulted from a spreading of the bacilli through the tracheal lymphatic pathway.

MAX PINNER.

OXIDATION AND REDUCTION AT THE SITE OF A TUBERCULOUS LESION. W. C. WHITE, M. I. SMITH and M. X. SULLIVAN, *Am. Rev. Tuberc.* **13**:77 (Jan.) 1926.

The nitroprusside test decreases in strength in direct proportion to the progress of a tuberculous process in a testicle. Methylene blue injections demonstrate a definite modification in the oxidation-reduction process at the site of a tuberculous lesion. Under some conditions the introduction to an area of tuberculous infection of an excess of such an oxidation-reduction mechanism as glutathione may grossly modify the process of the infection. Tuberculous foci show a definite acidity as compared with the alkaline reaction of normal tissue. All these observations lead the authors to the following

conclusions: "Since in the conjunction of the tubercle bacillus and the monocyte in their commensal existence, there are operating two different oxidation and reduction mechanisms—the monocyte in common with other body cells containing glutathione, the tubercle bacillus containing no glutathione, there is a possibility, in the competition of these two mechanisms for available labile hydrogen, of explaining the observed alteration in the structure of both organisms."

MAX PINNER.

THE ACTION OF UNSATURATED FATTY ACIDS ON TUBERCLE BACILLI. C. H. BOISSEVAIN, *Am. Rev. Tuberc.* **13**:84 (Jan.) 1926.

Tubercle bacilli in vitro are made to lose acid-fastness and virulence, and are apparently killed, by treatment with certain fatty acids of the aliphatic series, in full strength and in emulsion. Preliminary dehydration is not necessary. The effect seems to depend on the presence of a long carbon chain (5C) and a—COOH group, and to increase with the number of double bonds (degree of unsaturation), and the corresponding increase in solubility and power of being absorbed by the tubercle bacillus. Linoleic acid, the most effective fatty acid in vitro, has no effect on the course of tuberculosis in the guinea-pig. This may be due to the fact that in buffer solutions of pH 7 the acid is converted into soap, which is harmless to the tubercle bacillus.

MAX PINNER.

A METHOD FOR OBTAINING SINGLE COLONIES OF TUBERCLE BACILLI. C. H. BOISSEVAIN, *Am. Rev. Tuberc.* **13**:90 (Jan.) 1926.

Several methods are described to obtain single colonies of the tubercle bacillus. In all the mediums rabbit blood is used, which appears to contain some substance particularly favorable to the growth of tubercle bacilli.

MAX PINNER.

AN ATTEMPT TO ESTABLISH TISSUE-SPECIFIC STRAINS OF TUBERCLE BACILLI. L. M. DEWITT and H. G. WELLS, *Am. Rev. Tuberc.* **13**:92 (Jan.) 1926.

Guinea-pigs were inoculated through long series with tubercle bacilli from the same organs; thirty-five generations of inoculations, for example, were performed with a strain of bacilli from lymph nodes, thirty-eight generations were observed on a spleen series, etc. Over a period of nearly ten years no evidence was found that such strains develop any tissue-specificity.

MAX PINNER.

FOUR CASES OF TULARAEMIA (THREE FATAL) WITH CONJUNCTIVITIS. H. L. FREERE, G. C. LAKE and EDWARD FRANCIS, *Pub. Health Rep.* **41**:369, 1926.

Tularemia was demonstrated by animal inoculation and by cultural and serologic methods in the sole survivor of an outbreak of a glandular febrile affection with conjunctivitis occurring in four members of a family [Lee County, Va.], three of whom died without tests for tularemia having been made, either before or after death.

The four patients became ill within a twenty-four hour period, and, clinically, they constituted a group which presented the same symptoms and almost the same course and termination.

Although details as to the source and method of infection are lacking, there is abundant evidence of contact with rabbits, and the proof of the cause of illness of one of the group justifies the conclusion that all had tularemia.

Whether certain members of the family, in dressing infected rabbits, transferred the infection by their hands to their conjunctiva or whether insufficiently cooked rabbit was eaten, are matters of conjecture, but the evidence seems to point to primary infection of the conjunctivae.

AUTHORS' SUMMARY.

BACTERIOLOGY OF THE THYROID GLAND IN GOITER. A. CANTERO, Surg., Gynec. & Obst. 42:61 (Jan.) 1926.

Pieces of thyroid tissue from fifty goiters of the colloid and adenomatous types were cultured. In forty-seven of these bacterial growth was obtained. Streptococci were isolated in thirty-one, pneumococci in five, Welch's bacillus in two, staphylococci in seven, a diphtheroid bacillus, *Bacillus pyocyaneus* and *Micrococcus tetragenus* in one each. Isolated cultures of the streptococci were injected intravenously into rabbits. A variable degree of hyperemia and swelling of the thyroid were found in all. The organism was recovered from emulsions of the thyroid in all and from the blood in four of the animals.

N. ENZER.

BACTERIOLOGIC FINDINGS IN CHILDREN OF LEPERS: NASAL LESIONS. F. SOLIS and H. W. WADE, J. Philippine Islands M. A. J. S.: 365, 1925.

Of 250 children of lepers, 35 had lepra bacilli in the nose, but in not a single instance were nasal smears positive in the absence of skin lesions. The results indicate that nasal lesions are secondary manifestations in young children, and that the nasal mucosa is not frequently the site of the initial lesion in leprosy. Indeed, they suggest that, at least in young children, the initial lesion does not occur here at all, although there is reason to believe that occasionally such may be the case in older persons.

SPLENIC OPOTHERAPY IN TUBERCULOSIS. BAYLE, Arch. Int. de méd. expér. 1:483-503 (March) 1925.

Subcutaneous injections of spleen extract (glycerolized spleen extract 2 parts, physiologic salt solution 3 parts) seemed to be beneficial to tuberculous patients. An experimental control was advisable, and, according to the method of Schröder, Bayle studied the effect of splenic opotherapy in normal and in experimentally infected animals.

Hypermassive injections (2 cc. of extract per kilogram of body weight) produced a marked increase of the number of red blood corpuscles; the hemoglobin was higher; the leukocytes were also increased in number with lymphocytes predominating up to from 80 to 88 per cent.

Therapeutic doses (0.25 cc. of extract per kilogram of body weight) brought the same increase of red and white blood corpuscles; here, however, the relative number of polymorphonuclear cells is higher.

Guinea-pigs, infected by subcutaneous or intraperitoneal inoculation of human tubercle bacilli (2.5 cc. of a heavy suspension of bacilli per kilogram of body weight), and in which two therapeutic doses of spleen extract were injected every five days, lived much longer than similarly infected but not treated animals; they lost their weight more slowly. In the treated animals, many tubercles became sclerotic and fibroid, while in the nontreated animals the lesions were caseous and showed no tendency to heal. Splenic opotherapy impedes manifestly the evolution of experimental tuberculosis.

P. BRUTSAERT.

THE QUESTION OF THE RÔLE OF THE FLEAS OF SPERMOPHILES [GROUND SQUIRRELS] IN THE EPIDEMIOLOGY OF PEST. D. GOLOV and I. IOFF, *Rev. de microbiol. et d'épidemiol.* **4**:131, 1925.

The spermophiles of the Russian steppes harbor at least 3 species of fleas, of which two can bite persons. These fleas easily become infected with pest bacilli while feeding on spermophiles the blood of which contains the bacilli, and the bacilli multiply in the digestive tubes of the flea. Pest bacilli have been demonstrated in fleas for seventy-nine days, and the evacuations as well as the bite of fleas may be infective.

SYPHILIS INFECTION FROM CADAVER MATERIAL AND EVENTUAL PARASITISM OF *SPIROCHAETA PALLIDA*. E. HOFFMANN, München. *med. Wchnschr.* **73**:185, 1926.

Spirochaeta pallida multiplies in the cadavers of syphilitic persons for a considerable time, and may retain their virulence for several days. Seven certain cases and five probable cases of infection from this source are cited.

ARTHUR LOCKE.

RETICULO-ENDOTHELIAL REACTIONS IN EXPERIMENTAL TUBERCULOSIS. S. KAGEYAMA, *Beitr. z. path. Anat. u. z. allg. Pathol.* **74**:356, 1925.

Kageyama claims that India ink and bovine and avian tubercle bacilli, injected intraperitoneally, enter the lymph channels in the free state rather than within phagocytic cells as claimed by Goldmann and others. The injected material first reaches the retrosternal and tracheal lymph nodes, and only later and secondarily the other tissues and organs of the body. The peritoneal reaction to injected bacilli occurs in three successive stages which the author describes as a nonspecific leukocytosis, a specific histiocytosis and a lymphocytosis; whether the latter is specific or nonspecific could not be determined. Phagocytosis and digestion of the bacilli occur to a slight extent by leukocytes, chiefly by histiocytes, never by lymphocytes. In the lymph nodes, which the bacilli reach from the lymph stream, the earliest reaction consists of phagocytosis of the bacilli by the reticulum cells of the sinuses. Swelling and destruction of these cells occur somewhat later and lead to local leukocytosis. In the mouse the lungs become involved relatively late and are considered comparatively resistant to infection. The reaction within the lung consists at first of proliferation of alveolar epithelia which have enveloped the bacilli, and the lung is looked on as an important organ for the excretion of tubercle bacilli which have been injected intraperitoneally.

O. T. SCHULTZ.

A CONTRIBUTION TO THE PATHOLOGY OF TUBERCULOSIS OF THE HEART. W. STEFFER, *Ztschr. f. Tuberk.* **44**:199, 1926.

In 8 per cent of tuberculous children tuberculous lesions were found in the heart. This unusually high percentage is explained by the starved condition of these children (Russia). Chronic starvation results in a general atrophy of the heart. Of ten children with heart lesions, two showed isolated tubercles on the endocardium and on the pericardium, two had valvular foci and six myocardial lesions. The latter occurred in two different types: diffuse epithelioid infiltrations without caseation or diffuse infiltration with caseating tubercles. There is regularly observed a specific proliferation reaction of the capillary endothelium and subsequent epithelioid infiltration and a nonspecific reaction,

which is the phagocytic action of the newly formed cells. In cattle (four cases) the character of the cell infiltration in tuberculous cardiac lesions is not epithelioid, but fibroblastic.

MAX PINNER.

COSTAL CHONDRITIS FOLLOWING RELAPSING FEVER. B. E. LINBERG, Virchows Arch. f. path. Anat. **258**:367, 1925.

Relapsing fever, which became epidemic in Russia during the late war, was complicated during 1920, 1921, and 1922 by purulent osteochondritis of the ribs in an unusually large number of cases. The prevailing organism found by Linberg in his study of the condition was a paratyphoid B bacillus. The frequency of the complication in different parts of Russia appeared to bear a relationship to the distribution of paratyphoid bacilli, and the author considers the rib involvement to be the result of paratyphoid sepsis which became widespread as the resistance of the populace became lowered by hunger and starvation. From his histologic study of the involved cartilage he conceives the chondritis to be the result of bacterial embolism, the bacteria usually reaching the cartilage by way of the vessels which enter from the perichondrium. The first effect of the localization is central necrosis and liquefaction of the cartilage. This is followed by reactive proliferative inflammation of the perichondrium, in which new bone is formed. Penetration of the perichondrium leads to the formation of a chronic abscess. Involvement of the costal cartilages was also observed as a complication of typhus and typhoid fevers.

O. T. SCHULTZ.

INTESTINAL NECROSIS DUE TO ASCARIS. K. TAKEUCHI, Virchows Arch. f. path. Anat. **258**:502, 1925.

Takeuchi reports a case of fatal peritonitis in a 5 year old child, due to perforation of the intestine. In addition to the perforation there were numerous areas of sharply circumscribed necrosis in the intestinal wall, which involved the entire thickness of the wall and which were suggestive of pressure necrosis because of the absence of reactive phenomena in the tissue. Pressure by the large convoluted masses of *Ascaris* present was not believed, however, to be the chief factor in the necrosis, the action of toxins being considered more important.

O. T. SCHULTZ.

INTESTINAL CHANGES DUE TO THE DWARF TAPEWORM. N. KORNFELD, Virchows Arch. f. path. Anat. **258**:512, 1925.

Kornfeld could find only six previously reported cases in which *Hymenolepis nana* infection was found at necropsy. In three of these and in Kornfeld's case death was due to pulmonary tuberculosis, and in one was ascribed to the parasite itself. The infrequency with which the parasite is found at necropsy in spite of its frequent occurrence in the feces may be due to failure to see the parasite because of its small size or to disappearance of the parasites and spontaneous healing of the lesion. In Kornfeld's case, an adult aged 53, the parasites were found attached to the mucosa of the small intestine in extremely large numbers. The author claims that his is the first case to show the mode of attachment of the parasite, although the fixation of the closely related *Hymenolepis murina* of the negro has been described. The parasite causes numerous superficial ulcerations of the intestinal mucosa which are brought about by the loosening of its hooklets when it changes position. Recently ulcerated areas were hemorrhagic.

O. T. SCHULTZ.

ETIOLOGY OF LUNG GANGRENE. OLGA BYKOWA, *Virchows Arch. f. path. Anat.* 258:617, 1925.

Bykowa examined twenty fatal cases of lung gangrene with regard to the frequency of spirochetes and fusiform bacilli. She concludes that although initiation of the process may be due to a variety of causes, the rapid and widespread destruction of tissue is due to spirochetes. Subcutaneous injection into mice of material from pulmonary gangrene did not cause local gangrene unless spirochetes were present.

O. T. SCHULTZ.

TUBERCULOSIS AT VARIOUS AGES; ANATOMIC EXAMINATIONS. I. W. BLUMENBERG, *Beitr. z. klin. Tuberk.* 62:532, 1925.

A detailed report is made on postmortem examinations on 2,722 children up to 14 years of age with reference to tuberculous changes. A group of 163 cases was examined by the author, by hardening the organs in toto and sectioning them into 3 mm. thick slices. Of this group, seventy-five children (46 per cent) showed tuberculous foci. In thirty-nine tuberculous children the tuberculin test was negative ten times. In four tuberculin positive children a thorough macroscopic and histologic examination did not reveal any tuberculous changes. In 61.3 per cent of the author's group, the primary infection was in the lung. All the extrapulmonary primary foci were abdominal. In the order of frequency the primary focus was located in the right upper lobe (36.2 per cent), left upper lobe (24.8 per cent), right lower lobe (19.7 per cent), left lower lobe (15.7 per cent), middle lobe (12.6 per cent). In one third of the cases the primary focus was found to touch the pleura; in the other two thirds it was almost always only 2 to 10 mm. below the pleura. Histologically, the primary pulmonary focus is a caseous hepatization, encapsulated, without the formation of tubercles; it is mostly solitary, and is frequently changed into a cavity, particularly in infancy. An ascending infection of the cervical lymph nodes does not occur; in every case of cervical lymph node tuberculosis, a focus along the upper respiratory tract can be demonstrated. The regional lymph glands were found to be caseated the more the younger the child was. Complete caseation occurred in 95.8 per cent during the first year, and 27.7 per cent between the 10th and 14th year. Secondary intestinal tuberculosis was present in 39.8 and 56.5 per cent, respectively. Tuberculosis of the tonsils and of the larynx was found only in intestinal tuberculosis. Bone tuberculosis was never found in infants. In one fourth of the patients with primary abdominal focus, no lesion was detectable in the intestinal mucosa; the author believes that tubercle bacilli may pass the intestinal wall without producing any pathologic changes in it (primary tuberculosis of the mesenteric lymph nodes). Intestinal primary foci are in contradistinction to the pulmonary ones multiple, as a rule. The prognosis of the primary mesenteric tuberculosis is good, that of the primary intestinal tuberculosis is poor.

The most frequent form of thoracic tuberculosis between 14 and 20 years of age is the chronic pulmonary tuberculosis with tubercle formation in the regional lymph glands. A previous, healed tuberculosis is rare, and has apparently no influence on a tuberculosis in this age group.

MAX PINNER.

THERAPEUTIC ATTEMPTS WITH SANOCRYLIN. H. DEIST, *Beitr. z. klin. Tuberk.* 62:658, 1925.

Rabbits received 10 mg. sanocrysin per kilogram of body weight intravenously; in one group of animals this treatment was started simultaneously

with the infection, in one group fourteen days after the infection with virulent bovine tubercle bacilli. All animals died of extensive tuberculosis, the first group sooner than the controls. The author concludes that sanocrysin has no chemotherapeutic effect, but that it acts as a metallic poison. Small doses may exert a beneficial effect, not as a chemotherapeutic agent, but as a nonspecific stimulant.

MAX PINNER.

THE THERMOSTABLE BACTERICIDAL SUBSTANCES OF BLOOD SERUM. Y. IKEGAMI, Tohoku J. Exper. Med. **6**:567, 1925.

Human serum contains heat resistant substances that kill typhoid bacilli. Some animals (swine, dog) also have such substances. These substances are not influenced by artificial immunization. Evidence is presented that the bactericidal substances in the serum and in the leukocytes are identical, and that they do not occur in the organs.

Immunology

THE FATE OF REACTING LEUCOCYTES IN THE TUBERCULIN AND REINFECTION REACTIONS. FRED W. STEWART, PERRIN H. LONG and JOHN I. BRADLEY, Am. J. Path. **2**:47, 1926.

In the tuberculin and reinfection reactions in tuberculin hypersensitive animals, the reacting inflammatory cells themselves appear to be sensitized. Treated with appropriate doses of antigen, they undergo early death. These first cells are gradually replaced by others probably reacting largely to the presence of necrotic tissue. The newly emigrating cells are viable elements. Further study is required to determine the immunologic significance of these facts.

AUTHORS' SUMMARY.

A SUPRAVITAL STUDY OF LEUCOCYTES IN ALLERGIC STATES; A COMPARISON OF DELAYED AND IMMEDIATE INTRAPLEURAL ANAPHYLACTIC REACTIONS. PERRIN H. LONG and FRED W. STEWART, Am. J. Path. **2**:91, 1926.

In the delayed intrapleural anaphylactic reaction in rabbits sensitive to horse serum, reacting leukocytes are largely killed. In this respect, the reaction parallels the intrapleural tuberculin reaction in guinea-pigs. Attempts to induce an immediate intrapleural anaphylactic reaction in rabbits resulted in no apparent cell injury. In sensitized guinea-pigs no cell injury either immediate or delayed was observed when antigen was introduced into the pleural cavity. Evidence gleaned from this study accords well with facts already known about delayed and immediate anaphylaxis.

AUTHORS' SUMMARY.

INTERAGGLUTINATION OF MATERNAL AND FETAL BLOOD IN THE LATE TOXEMIAS OF PREGNANCY. WILMAR M. ALLEN, Bull. Johns Hopkins Hosp. **38**:217, 1926.

The iso-agglutination characteristics of the blood specimens of 375 normal and of 104 toxemic women and their newly born infants have been studied.

There is no evidence that incompatibility is more frequent in toxemic than in normal gestation. Incompatibility between the blood of mother and infant was present in 20.8 per cent of 375 normal and 21.1 per cent of 104 toxemic pregnancies. There is no evidence of an increased agglutinin titer in the maternal serum of toxemic women. There is no evidence of specific immunization of the mother against fetal corpuscles.

The discrepancy between this and previous work is probably accounted for by the size of the series studied. With a small number of cases the percentage of error and likelihood of coincidence are very great. The study of this series of cases, by the methods used, gives no evidence that the late toxemias of pregnancy have their origin in iso-agglutination phenomena.

AUTHOR'S SUMMARY.

SKIN REACTIONS WITH FILTRATE OF KOCH STRAIN OF BACILLUS TUBERCULOSIS.

RUSSELL D. HERROLD and CLARENCE C. SÆLHOF, J. A. M. A. 86:747, 1926.

Intradermal injections of 0.1 cc. of filtrate dilutions up to 1:50 were made. In most of the adults receiving injections in this way a definite skin reaction developed. In patients with active tuberculosis no reactions developed. In a series of children convalescing from acute infectious diseases the results were mostly negative. The results appear to warrant further work with filtrates of cultures of various strains of the tubercle bacillus.

TESTICLE INFECTION IN GUINEA-PIGS SENSITIZED WITH KILLED TUBERCLE BACILLI.

F. W. STEWART, J. Immunol. 11:123, 1926.

A positive intradermal reaction to old tuberculin diluted with 19 parts of physiologic saline may be obtained in guinea-pigs previously receiving injections with certain amounts of killed tubercle bacilli. Subsequent testicular infection with the B-1 strain of tubercle bacillus in a sensitized animal within forty-eight hours causes slight edema, a heavy deposit of fibrin, a marked infiltration by polymorphonuclear leukocytes, many eosinophils, mitoses in endothelial leukocytes and in fixed endothelial cells. The germinal epithelium becomes vacuolated, many immature cells slough off into the lumina of tubules, often forming multinucleated epithelial giant cells. Tubules of the epididymis become filled with immature sex cells, polymorphonuclear leukocytes and phagocytic endothelial leukocytes. The control animal exhibits a slight infiltration by polymorphonuclears, eosinophils, lymphocytes and endothelial leukocytes. A trace of fibrin, no edema and a normal epithelium characterize early stages. Mitoses are seen in endothelial leukocytes and fixed endothelium; in other words, the sensitized animal shows a much greater exudative reaction and a more marked, though not earlier, proliferative (endothelial) reaction. Necrosis of tubules and possible thromboses cannot be excluded as important factors in the initiation of a marked polymorphonuclear reaction in the sensitized. Hemorrhage may occur in the sensitized testis. Abscesses occur both in sensitized and control animals. They appear earlier and are larger and more numerous in the sensitized testis. Phagocytosis of polymorphonuclear leukocytes by endothelials occurs in both and varies with the number of polymorphonuclears present in the exudate. An eosinophil reaction occurs in both control and sensitized, is inconstant, and tends to disappear as the tuberculosis progresses. It cannot be shown to be associated with sensitization. As the disease progresses, the architecture of the testis becomes disorganized—much earlier in the sensitized than in the control. Tubules are gradually lost, their cells becoming indistinguishable in masses of polymorphonuclears, endothelial leukocytes, giant cells and fibroblasts. Remnants of tubules may persist as bright eosin-staining débris in the midst of such masses. Much of the epithelium undergoes phagocytosis. Proliferation of fibroblasts occurs earlier and to greater extent in the sensitized testis, but occurs in the control before a positive skin reaction is obtained. Every histologic characteristic of the sensitized testis, though to lesser degree, may be encountered in the control testis before the

intradermal test has become positive, and in consequence no one histologic feature may be said to characterize the reaction to reinfection in the testis of an animal generally sensitized to tuberculin. The differences are only those of degree, both in time and in amount of exudate and proliferative reactions. The presence of early necrosis in the sensitized testis makes it impossible to decide whether the acuteness of reaction is a more rapid formation of "protective" tissue or a response to necrosis. The two may not be mutually exclusive. After the sixth day, little or no difference is seen between control and sensitized animals. Eventually caseation occurs in both. In this series it was not shown that sensitization has any protective value; in fact, the controls showed rather less disease. The foregoing conclusions apply to a given organ, given sensitization, and to a certain infecting quantity of the B-1 strain of tubercle bacillus. They must be interpreted only as such.

S. A. LEVINSON.

THE ANTICOMPLEMENTARY REACTION OF BLOOD SERUM OR OF SPINAL FLUID.

A. H. SANFORD, *J. Lab. & Clin. Med.* **11**:413, 1926.

An anticomplementary reaction of fresh serum, or spinal fluid, occurs with the Kolmer modification about twice in each thousand tests. This reaction is not specific for syphilis, although it occurs more often in syphilitic than in nonsyphilitic cases. Its occurrence with spinal fluids may be indicative of severe syphilitic involvement of the central nervous system. The nature of the anticomplementary substance has not been fully determined. It does not seem to be due to natural antigen in the serum, or spinal fluid itself. It is transient in character in some cases, and in others is found constantly. Quantitatively it is not as active as is the complement-fixing property of syphilitic serum when antigen is added.

S. A. LEVINSON.

IMMUNIZATION AGAINST PNEUMONIA. RUSSELL L. CECIL, *Medicine* **4**:395, 1925.

An attack of pneumococcus pneumonia confers on the patient a high immunity against the particular type of pneumococcus with which he has been infected. A small amount of cross-immunity is simultaneously established against the other types.

By the injection of killed or living cultures of pneumococcus, it is possible to obtain an active immunity against the homologous type of pneumococcus. This immunity is evidenced in laboratory animals by the animal's resistance to infection and by the presence of various immune bodies in the circulating blood.

Subcutaneous, intravenous or intratracheal injections of pneumococcus vaccine produce in monkeys an active immunity against experimental pneumococcus pneumonia of homologous type.

Pneumococcus vaccine when given in adequate doses confers immunity against pneumococcus pneumonia in man. The evidence in favor of such immunity rests on statistical studies and on the demonstration of immune bodies in the blood of those vaccinated.

The chief indications for the use of pneumococcus vaccine at the present time are: first, to prevent recurrence in individuals who are highly susceptible to repeated attacks of lobar pneumonia; second, for the prevention of outbreaks of pneumonia among fresh recruits in training camps.

There is reason to believe that the recent isolation of certain derivatives of the pneumococcus which contain the antigenic principle will eliminate the

undesirable features of vaccination against pneumonia and thereby render the procedure more practical in civil life.

AUTHOR'S SUMMARY.

ALLERGY: A PATHOGENIC AND THERAPEUTIC STUDY. DUJARDIN and DESCAMPS, Arch. Int. de méd. expér. 1:539-575, 1925.

Taking as a basis the existence or the absence of allergy, one can rationally classify the different forms of syphilis into three: (a) an early or primo-secondary anallergic syphilis; (b) a tertiary or allergic syphilis; (c) a late anallergic syphilis, containing at the same time the late secondary syphilis and the so-called parasymphilis of Fournier.

When allergy appears in syphilis, the observed hypersensitiveness, tested by intradermoreaction, is not limited to the specific substances such as luetin and pallidin, but is extended to all kinds of substances, for example, to tuberculin, (Dujardin) extracts of normal liver (Neisser and Bruck), Noguchi's culture medium without spirochetes, cow's milk, etc. Dujardin and Duprez showed that in tuberculosis the patients react allergically not only to tuberculin, but even to cow's milk and to horse serum (reaction of Bursaca). It seems well demonstrated that some infections besides a specific hypersensitiveness (allergy) produce a nonspecific hypersensitiveness. Dujardin and Duprez suggest naming the latter hetero-allergy.

It is known that we can treat successfully primary and secondary syphilis. In tertiary syphilis, it is noticeable that success is gained by our medicines in the allergic but not in the anallergic syphilis. The question then arises: Should we not try to change the anallergic cases into allergic? By injecting horse serum or cow's milk, we can perhaps produce a hetero-allergy to spirochetes, which hetero-allergy may have the same effect as allergy in tertiary cases.

Injecting intradermally 0.2 cc. of pure and aseptic horse serum, Dujardin observes that the capacity for allergy varies greatly in man. In the greatest number of cases, one intradermal injection is sufficient to create a marked hypersensitiveness to horse serum at the eighth day. On the contrary, some persons have only a slight tendency to allergy while others have no tendency.

In the former cases, parallel to the increased susceptibility to horse serum runs an increased susceptibility to cow's milk and to tuberculin; in the latter, when repeated injections of horse serum did not produce any hypersensitiveness, there was also absence of increased susceptibility to milk and to tuberculin.

In several cases, there was no parallelism. Patients receiving injections with horse serum who showed hypersensitiveness against horse serum and cow's milk but not against tuberculin, never acquired any allergic state against it. Hetero-allergy influences only the susceptibilities already present.

Proteinotherapy in cases of syphilis that were resistant or became resistant to the classic treatment, gave many good results; in many cases it failed. These results are to be expected, since we know that the action of proteinotherapy depends essentially on the capacity for allergy of the patient, and this capacity has been shown to vary greatly in different persons.

PAUL BRUTSAERT.

THE MEINICKE MICRO-REACTION. J. BURTSCHER, München. med. Wchnschr. 73:192, 1926.

A micro-adaptation of the Meinicke flocculation reaction is described in which the serum and the Meinicke extract are mixed in capillary tubes and the occurrence of flocculation detected microscopically in hanging drops.

ARTHUR LOCKE.

CONTRIBUTION TO THE STUDY OF IMMUNE PHENOMENA IN FEMALE STERILITY. G. J. SEBASTIANINI and G. LAUSI LIBERATI, "Zacchia" 4: 1925.

In a small series of experiments results were obtained indicating that injecting into female guinea-pigs glycerole extract of guinea-pig testicle produced temporary sterility. In the serum of the animals receiving injections precipitins developed for the proteins in the testicular extract. It is reported, further, that the serum of prostitutes and of pregnant women contain agglutinins for human spermatozoa.

THE PRECIPITINS OF HEMOGLOBINS. TETSURO ISHIKAWA and KAKUZO SAKURABAYASHI, Tohoku J. Exper. Med. 6:395, 1925.

The results show that in specific precipitation of hemoglobin it concerns the protein part only.

I. THE STUDIES ON THE MENINGOCOCCI VARIABILITY OF MENINGOCOCCI. II. CLASSIFICATION OF MENINGOCOCCI ON BASIS OF AGGLUTININS. III. RELATIONSHIP BETWEEN AGGLUTININ REACTION AND SUGAR FERMENTATION. S. KONDO, Tohoku J. Exper. Med. 6:399, 1925.

The changes in the agglutinability of meningococci depend on the development of variants that resist agglutination. In order to maintain a strain of constant agglutinability, it is necessary to transplant from a colony that is found to be agglutinated in typical fashion by the homologous serum.

By the use of serum produced with pure strains as described, Kondo found that forty-three meningococcus strains could be divided into thirteen types, which does not represent, however, all the types of meningococcus in nature.

Kondo found that while meningococci may be divided into groups according to their power to ferment levulose, maltose and dextrose, yet these groups do not correspond with serologic groups.

Tumors

CAVERNOUS HEMANGIOMA OF THE BLADDER. HARRY KATZ, J. Urol. 15:201, 1926.

Ten cases of cavernous hemangioma of the bladder are found in the literature. Of these, three were confirmed by microscopic examination. Another case is reported, which was verified by necropsy and microscopic examination.

AUTHOR'S SUMMARY.

SARCOMATOSIS OF THE BRAIN. B. M. FRIED, Arch. Neurol. & Psychiat. 15:204, 1926.

A man, aged 33, suddenly became ill with symptoms of a brain tumor which could not be localized. He died two months after the onset of the first symptoms; necropsy showed to the naked eye merely a small tumor nodule, but the microscope revealed the widespread presence of tumor cells throughout the entire cerebrum, cerebellum, pons, medulla oblongata and meninges. The growth proved to be composed of small, round cells which showed numerous mitotic figures, and had a definite perivascular arrangement. The parenchyma and interstitial tissue of the brain showed extensive secondary degenerative changes.

Differential diagnosis lies between a metastasis and a primary tumor of the brain with diffuse extension. Tumor cells undergoing mitoses occurred in

the adventitia of vessels possessing an intact tunica intima, intima piaie and limitans gliae. It is shown that the tumor cells were not of glial, nervous or ependymal origin. It is believed consequently that the tumor originated from the adventitial cells of the Virchow-Robin spaces, in other words, from the mesenchymal element of the brain, and it therefore is regarded as a primary sarcoma of the brain of connective tissue origin.

AUTHOR'S SUMMARY.

LYMPHANGIOMATA OF THE FALLOPIAN TUBE: TWO CASES. L. W. STRONG, *Am. J. Obst. & Gynec.* 10:853 (Dec.) 1925.

Strong reports two cases of lymphangioma of the fallopian tubes. The lesions were small nodules, which consisted of spaces lined with flat endothelial cells. Only five such cases have been previously reported. There was no association of uterine myoma in the cases here described.

A. J. KOBAK.

THE ANATOMICAL DISTRIBUTION OF THE OCCUPATIONAL CANCERS. E. L. KENNAWAY, *J. Indust. Hyg.* 7:69, 1925.

This careful and thorough review of occupational cancer in workers with mineral oils, coal tar and the products of its distillation, is based on vital statistics of England and Wales. It concerns 921 deaths from cancer of the scrotum and penis during five years; reports from the Inspector of Factories of 144 cancers in 133 persons, the cancers being due to coal tar and the pitch it yields; cancer in chimney sweeps and the occupations of 141 patients of an infirmary in Manchester who had scrotal cancers. There is also a good review of literature with summaries of observations made in continental Europe, the contributions from America apparently being very few in proportion to the number engaged in industries implicated.

Notwithstanding the strength of the arguments presented for the great ease with which foreign substances find lodgement in the rugose skin of the scrotum, no explanation altogether satisfactory has been found for the frequency of scrotal cancer among these workers.

Coal tar and its products cause cancer of the head and neck, and of the hands and forearms about as frequently as of the scrotum, but in certain workers, "mule-skinners," whose clothing covering the lower part of the abdomen and upper part of the thighs becomes soaked with oil, the scrotum is almost solely the part where cancer develops.

The growths are often multiple and wartlike, with, for example, two separate carcinomatous epitheliomas of the scrotum in addition to a number of papillomas; or growths may develop on both the scrotum and neck or face, or on the forearm and wrist.

Among paraffin workers, as many as thirteen or sixteen years may elapse before cancer develops, or its character may first be manifest a number of years after change to an occupation devoid of cancer hazard.

According to Kennaway, cancer among chimney sweeps is as prevalent as ever. The cancers due to coal tar and its products are regarded as analogous in some measure to those of the urinary bladder among workers with aniline and its derivatives, the growth-inciting substances for the bladder tumors being formed or set free during excretion of what is absorbed.

Some oils were found capable of causing cancer only after subjection to high temperatures.

The possible relation of these occupational cancers to the employment of mineral oil as a laxative is not mentioned.

Cancer of the penis is connected with repeated applications to that part of the oils under discussion during urination, and there is certainly no limit, apparently, to which measures of cleanliness should be observed by laborers in the industries discussed.

E. R. LeCOUNT.

MALIGNANT CHANGE IN TUMOR OF RECTO-GENITAL POUCH. S. BARNES, A. P. THOMPSON and A. W. LAMB, *Quart. J. Med.* **74**:155, 1926.

This is a case report of sarcomatous change in an adenomyoma of the pouch of Douglas, with extensive metastases to the lung. The clinical signs were those of cyanosis and erythema, postulated as being due to insufficient oxidation of the blood caused by the diffuse permeation of the alveolar septums by the metastases.

N. ENZER.

THE CLASSIFICATION OF CEREBRAL TUMORS. ROUSSY, LHERMITTE and CORNIL, *Ann. d'anat. path. med.-chir.* **1**:333, 1924.

The present classifications of cerebral neoplasms are founded on embryologic concepts, although these must not be taken too seriously, since they rule out the pathogenesis, embryologic displacements and traumatic factors, and commit one to the "dysembryoblastic" theory of tumor formation. A short discussion of the histogenesis of the central nervous system is followed by a similar one on the cytology, histology and regional variations of the neuroglia. The authors divide tumors of the interstitial tissue of the brain into (1) astrocyte gliomas or astrocytomas; (2) cellular or nonfibrillar gliomas, including such varieties as the round cell, spindle cell, polymorphic, and ameboid cell gliomas; (3) glioblastomas and spongioblastomas or ependymogliomas.

The astrocytoma, the most common tumor, is composed of cells which retain many characteristics of adult neuroglia. The cytoplasm of the constituent cells contain from 2 to 30 glia granules; the nucleus, generally rounded, sometimes elongated, seldom mitotic, has a distinct chromatin network. In various locations, very large degenerated cells are often seen. Neuroglia fibers are seen in great abundance, especially in the hard or fibrous tumors. Nerve cells and fibers may be found within the confines of the tumor. The mesodermic tissue is increased, with the presence of large almost cavernous blood vessels. Thromboses, hemorrhages and other degenerations are by no means rare. There is no reciprocal mutation between ectodermic and mesodermic tissue, however. The collagen, at times found in large amounts, is laid down both by the physiologic activity of the perivascular sheaths and by precipitation of certain proteins in situ. The vessel walls often undergo hyaline or even calcareous degeneration.

The nonfibrillar gliomas comprise two main types, those with round cells and those with spindle cells as a basis. The small round cells are distinguished from lymphocytes by their paler nuclei. The whole tumor is composed of these cells and much resembles the small round cell sarcoma which arises in the brain only as a metastasis. Blood vessel walls are very thin, though not seldom hyalinized. The spindle cell glioma is even more likely to be confounded with sarcoma, although the separation has been accomplished satisfactorily by the use of elective methods of impregnation. The cells of this tumor are united in a vast syncytium within which the cell boundaries are no longer recognizable. The slender nuclei, pale, with few chromatic granules,

never take on extraordinary proportions. Arranged parallel with one another, the cells are gathered in large sweeping bundles which run in different directions. In other locations the groundwork may appear reticular, with stellate cells, anastomosing with one another. This tumor is found most frequently on the cranial nerves.

The polymorphic cell glioma is recognized by the wide variation in the types of cells present and by the occurrence of giant forms. In these last the nuclei can sometimes be seen joined to one another by fine chromatic bands, recalling the structure of the polymorphonuclear leukocyte.

The ameboid cell gliomas are distinguished from the preceding by their cellular structure. These elements have an abundant cytoplasm, with long branching projections often joined to expansions of contiguous cells. The cytoplasm is clear, often vacuolated, containing fat globules, products of disintegration of the myelin sheaths and other granules. Nuclei are situated eccentrically; they are small, dark, with a definite nuclear membrane. These tumor cells extend into the surrounding tissue without definite limits, the neoplastic cells coming to resemble more and more the normal tissue cells, until they merge directly with the normal neuroglia.

Degenerative processes are often observed in all gliomas. These comprise hemorrhages from the large cavernous delicate vessels, colloid degeneration and cyst formation. The latter is due to the colloid degeneration of both cell and stroma in the tumor.

Tumors of the ependyma and choroid plexus can be differentiated when the cells have reached adult type, but since they spring from the same cell, that lining the neural canal, the differentiation of less developed forms is often difficult. These tumors arise in the juxta-ependymal region, and often when no tumor exists we may find enclosed in the nervous substance some acini and rosetts, probably snared off from the ependyma in the vicinity.

An interesting section is devoted to the cerebral lesions arising as a consequence of the development of gliomas in the brain. The glioma itself destroys the nerve tissue only slightly, not nearly to the extent that a vascular lesion does. Rather it displaces the nervous tissue. Even the compression, however, is harmful in the end, probably by bringing about interference with effect by altering the circulation of the cerebrospinal fluid, especially that flowing about the individual cells. Even so, the degeneration is much less marked than one would expect from the volume of the tumor. The production of hydrocephalus and displacement of the basilar structures through the foramen magnum are touched on, but more particularly the lesions in the vicinity of the tumor. On fresh section the pallor and flattening of the convolutions are to be remarked, then the brownish discoloration, the disappearance of the subarachnoid space. Under the microscope the nerve fibers appear swollen, with fragmentation of the myelin and thinning of the sheath. Fat may be abundant as a result of myelin destruction. At other times the sheath is swollen, the interstitial tissue manifests a notable reticulum, and ameboid cells proliferate and take up the products of disintegration. Perivascular spaces are dilated and contain phagocytic cells, especially polyblasts, but no plasma cells. The ganglion cells in the vicinity show chromatolysis, displacement of the nucleus, condensation of the dendrons, and often marked satellitosis. Such cellular changes are often found at a considerable distance from the neoplasm and may explain the psychic symptoms, especially the progressive deterioration. Whether they are due to intoxication from the by-products of metabolism of the tumor cells or to interference with nutrition cannot be answered positively.

Certain tumors in the central nervous system undoubtedly spring from the nerve cells. Although adult nerve cells never proliferate, the immature ones possess this capacity, and from them spring certain rare tumors—the ganglioneuromas, the neurogliocytomas, the neuroblastomas and so on. In these tumors are found rather large cells with more or less the appearance of chromophilic granules, intracellular fibrils and building axons, all in a primitive stage of development. Grossly these tumors resemble the ordinary gliomas. Closely allied to these remarkable tumors are the congenital malformations, such as disseminated cortical histio-atypia, tuberous sclerosis, pseudosclerosis, etc.

Tumors developing from the cranial nerves have been considered as fibromas, or neuromas. The most common are those developing on the acoustic nerve. These spring from the peripheral neuroglia which, outside the cranial cavity, become the cells of Schwann. Since it has been shown that the so-called neuromas in the peripheral nerves arise from the cells of Schwann, they may well be termed peripheral gliomas. The same holds true for the tumors developing on nerves within the cranial or spinal cavity. The tumors resemble the fusiform gliomas in practically every detail.

When multiple tumors spring from the nerves, the question of simultaneous origin or metastasis arises. When the tumors are of approximately equal size, as often happens in the acoustic area, they may be considered as independent; when, however, there is a multitude of such small tumors, metastasis by way of the spinal fluid is more likely. This condition is closely allied to the "neurofibromatosis" of von Recklinghausen, although the prognosis is much less favorable.

A considerable and useful bibliography is appended.

FREEMAN.

RETICULUM OF CARCINOMA AND SARCOMA. H. EDELMANN, *Virchows Arch. f. path. Anat.* **258**:317, 1925.

Edelmann applied the Bielschowsky-Maresch method to carcinomas and sarcomas for the purpose of studying the relation of the reticulum to the tumor cells. He concludes that the method has differential diagnostic value but is not absolute, because reticulum may be absent in cellular sarcomas as it is in medullary carcinomas.

O. T. SCHULTZ.

PAPILLARY EPITHELIOMA OF CHOROID PLEXUS. KLARA NOODT, *Virchows Arch. f. path. Anat.* **258**:351, 1925.

Noodt reports a papillary epithelial tumor of the choroid plexus of the left lateral ventricle in a man aged 33 years and a similar tumor of the third ventricle in a boy aged 1 year.

O. T. SCHULTZ.

RHABDOMYOMA OF HEART. E. UEHLINGER, *Virchows Arch. f. path. Anat.* **258**:719, 1925.

Uehlinger reports a case of diffuse rhabdomyoma of the heart in a man, aged 20. Renal or other anomalies, which are so frequently associated with this type of tumor, were absent.

O. T. SCHULTZ.

Medicolegal Pathology

DEATH FOLLOWING THE INHALATION OF ZINC STEARATE. KARL SCHLAEPFER, *Am. J. Dis. Child.* **31**:474, 1926.

A child, aged 7½ months, died thirty-four hours after the inhalation of zinc stearate. Cyanosis and dyspnea characterized the clinical course of the illness, and a state of "acidosis" was noted after the patient was admitted to the hospital, twelve hours before death. At necropsy, the lungs were voluminous. Extensive areas of emphysema were separated from each other by small, scattered, atelectatic zones. The bronchioles contained plugs of zinc stearate and mucus, which appeared as wormlike masses. The gross picture was confirmed histologically, and the presence of extensive edema was determined. The edema involved the alveoli, especially the more atelectatic ones, and the subpleural and interlobular connective tissue septums. The lymphatics throughout the lung were conspicuously dilated.

In spite of oxygen inhalation, persistence of the dyspnea may have been due to acidosis brought about by incomplete obstruction to the bronchioles with zinc stearate.

AUTHOR'S SUMMARY.

WHITISH GRANULATIONS IN CADAVERS. C. STRYZOWSKI, *Presse méd.* **33**:353 (March 18) 1925; *abs., Ann. de méd. légale* **5**:163 (April) 1925.

This concerns the elevated, verrucous, whitish spots, of variable extent, which arise on the surface or in the interior of certain organs of cadavers. Chemical examination reveals tyrosine. Production of this amino-acid is apparently due to autolysis, analogous to that which occurs when certain organs are subjected to aseptic autolysis. One must avoid confusion with calcium soaps (adipocere). This fact, which should be known in legal medicine, is worthy of note by those who study the phenomena of putrefaction.

B. R. LOVETT.

SPONTANEOUS OR TRAUMATIC RUPTURE OF THE UTERUS. A. HABERDA, *Wien. med. Wchnschr.* **39**:32, 1926.

The formal complaint to the local authorities by a husband charged that the physician refused to accompany him to his home when his wife was desperately ill in child-birth unless he provided a conveyance; that when they finally arrived there delayed by the refusal mentioned, the physician was in too great haste, did a forceps delivery and crushed the child's head; that the physician then tore out the afterbirth violently, leaving part of it in the womb, and that in these ways the physician was responsible for the death of the wife.

The postmortem examination made by a commission selected by the local court disclosed an extensively torn cervical portion of the uterus, a generalized acute peritonitis and evidence of rickets. No measurements were made of the bone boundaries of the birth passage, and when the reports came to Haberdar in a routine way for him to pass on the entire affair officially, he commented on this neglect as a notable omission.

The physician was completely exonerated through his deposition and that of the midwife establishing spontaneous rupture of the uterus with hemorrhage and abrupt cessation of severe labor pains before the arrival of the physician; that haste in delivery was clearly indicated, and that the peritonitis was due to infection by way of the tear of the uterus and not a result of incomplete removal of the placenta.

E. R. LeCOUNT.

Technical

- A QUANTITATIVE METHOD FOR THE DETERMINATION OF THE COMBINED UREA AND AMMONIA NITROGEN OF SALIVA. FREDERIC W. SCHLUTZ and MILDRED R. ZIEGLER, *Am. J. Dis. Child.* **31**:520, 1926.

The method is a modification of the method for determining blood urea in Folin's Laboratory Manual of Biological Chemistry, and it is of especial value because saliva is easier to collect than blood. It will be recalled that combined urea and ammonia nitrogen run closely parallel in blood and saliva. In the method described 10 cc. of saliva is collected without the use of any stimulant.

- A MICROSCOPIC SLIDE PRECIPITATION TEST FOR SYPHILIS. B. S. KLINE and A. M. YOUNG, *J. A. M. A.* **86**:928, 1926.

A microscopic modification of the Kahn test is described. The test is simpler and easier to read than the regular three tube Kahn test.

- A NEW METHOD FOR THE IDENTIFICATION AND ESTIMATION OF CHOLESTEROL AND CERTAIN OTHER COMPOUNDS. J. V. STEINLE and L. KAHLENBERG, *J. Biol. Chem.* **67**:425, 1926.

A chloroform solution of antimonie chloride (SbCl_3) forms a muddy brown precipitate with dilute solutions of cholesterol. The precipitate dissolves in more chloroform to a clear, purple liquid which changes to a cobalt-blue on exposure to light. A simple addition compound is formed between the antimony chloride and the cholesterol, and its definite composition permits the use of the reaction for the quantitative estimation of cholesterol.

ARTHUR LOCKE.

- SPECIFIC INFECTIOUS CYSTITIS AND PYELONEPHRITIS OF COWS. F. S. JONES and RALPH B. LITTLE, *J. Exper. Med.* **42**:593, 1925.

A specific infection of the urinary tract associated with a diphtheroid infection has been encountered in cows from three dairy herds. The most characteristic symptom is the frequent passage of turbid or blood stained urine. The bladder was always found to be involved. The bladder walls were thickened, the mucosa swollen and reddened. Patches of exudate adherent to the bladder mucosa were frequently observed. In certain instances one or both ureters were thickened. In other cases one or both kidneys were involved. The kidney process seemed to originate in the pelvis and extend toward the medulla and cortex. The characteristic bacilli were always found in large numbers in the urinary sediment and the pelvis of involved kidneys.

AUTHORS' SUMMARY.

- A NEW CONTAINER FOR TUBERCLE BACILLI CULTURES. K. LANKEN, *Beitr. z. klin. Tuberk.* **62**:707, 1926.

This is a description of a wide-mouthed bottle with a narrow lateral tube, through which seeding is done. This container is recommended as equally suitable for solid and liquid mediums.

MAX PINNER.

- CONCERNING THE EXISTENCE OF CYTOTOXINS. K. A. FRIEDE, *Centralbl. f. Bakteriol. I. O.* **96**:141, 1925.

Of all the specific cytotoxins described in the literature, only hemolysin and spermatolysin, the activity of which can be demonstrated in vitro, are to

be regarded as true cell toxins. The same changes are caused in the animal body by normal or immune serum, organ extracts, etc., as are attributed to the specific effects of cytotoxins. In immunizing an animal A with cells from any organ of an animal B, antibodies are formed, not against cells of the same organ, but against all proteins of the animal B.

B. R. LOVETT.

WASSERMANN REACTION IN CHILDBIRTH. I. AVAILABILITY OF RETROPLACENTAL BLOOD. H. BOAS and GAMMELTOFT, *Hospitaltid.* 69:49, 1926.

II. IS VENOUS BLOOD OF PARTURIENT SUITABLE? H. BOAS, GAMMELHOFT and K. LICK, *ibid.*, p. 61.

Retroplacental blood may give nonspecific response to serologic tests for syphilis. Positive Wassermann reactions with blood serum obtained in the usual way from parturients may be regarded as dependable. The Wassermann reaction is as dependable in pregnancy and childbirth as at other times.

Society Transactions

INTERNATIONAL ASSOCIATION OF MEDICAL MUSEUMS

*Report of Meeting Held at the Division of Laboratories and
Research of the New York State Department of Health,
Albany, N. Y., April 1, 1926*

The following officers and council were elected: president, James F. Coupal, Washington, D. C.; vice-president, Howard T. Karsner, Cleveland; councilors, Oscar Klotz, Toronto, James Ewing, New York, Stuart Graves, Louisville, F. B. Mallory, Boston, V. C. Jacobson, Albany, E. B. Krumbhaar, Philadelphia, A. S. Warthin, Ann Arbor, F. D. Weidman, Philadelphia, G. R. Callender, Washington, D. C., Ward Mac Neal, New York, R. W. French, Washington, D. C.; secretary-treasurer, Maude E. Abbott, Montreal.

Dr. Maude E. Abbott on behalf of the committee on publication presented the completed Bulletin IX, "Appreciations and Reminiscences of Sir William Osler, Bart., with a Classified Annotated Bibliography."

DEMONSTRATION EXHIBITS

Pathogenesis of Menstruating Ovarian Cysts and Peritoneal Endometriosis. Photograph and drawings. John A. Sampson, Albany.

Experimental Endometriosis in Rabbit and Monkey. V. C. Jacobson, Albany.

Endometrial Growth in Right Labium Majus. J. Stewart Henry, Montreal.

Series of Cultures of the Common Ring Worm. J. Burgess, Montreal.

Specimens Mounted by Shore's Method. Helen Ingleby, Philadelphia.

Pathology of the Eye and other Conditions of Interest. G. R. Callender, Army Medical Museum, Washington.

Paintings and drawings illustrating various pathological lesions. L. J. Rhea, Montreal.

Histotopography of Organs. Erwin Christeller, Berlin, Germany.

Pneumococcus Endocarditis in the Horse Following Immunization with Pneumococci. J. McKinnon, Albany.

A motion picture film of heart studies by Dr. E. A. Libman of New York, and loaned by Mr. Paul B. Hoeber, was shown.

Microscopy of the Living Eye. W. G. M. Byers, Montreal.

Injection of the Placental Circulation. D. Kearns, Montreal.

Lesions of Peripheral Blood Vessels in Rheumatism. A. M. Pappenheimer, New York.

Some Unusual Findings in the Vermiform Appendix. A. Plaut, New York.

Myocardial Changes in Cardiac Defects. Maude E. Abbott, Montreal.

SCIENTIFIC PAPERS

THE PRESERVATION OF COLOR IN GROSS SPECIMENS: INFLUENCE OF P_n OF PRESERVING FLUIDS. G. R. CALLENDER and H. A. DAVIS, Washington.

Sections of fresh rabbit lung were fixed in Kaiserling's fluid of varying p_n , and it was found that a slightly acid reaction gave the most permanent coloring in Kaiserling III plus 4 per cent sodium arsenate; p_n 6.5 gave the

best results. Illuminating gas used with Kaiserling I apparently eliminates the necessity of using alcohol in the second step. The sodium arsenate prevents the formation of molds, in the experience of the Army Medical Museum.

THE TAKING OF SECTIONS FOR MICROSCOPIC SLIDES. E. L. JUDAH, Montreal.

To overcome the unnecessary disfigurement of museum specimens at post-mortem or in the operating room, the following method of cutting bits of tissue for microscopic examination has been found to work satisfactorily, and does away with the square, ragged hole so often seen in museum material. It also materially helps the museum technician in mounting museum material.

Method.—There are, in all, three differently shaped blocks which can be taken without disfiguring the specimen, shown as follows: (1) a thin slab cut from a flat surface when the organ has been laid open to examine in the gross; (2) a wedge, or "V" shaped piece when it is necessary to include part of the surface; (3) a lens shaped section which can be taken from the center of any specimen without disfiguring it. Whenever possible, this should be taken from the back of the organ, making a clean cut through to the front surface.

In the two latter methods, the hole made should be closed by individual sutures as soon as possible, so that when the specimen is hardened, it will be practically indistinguishable.

When a section has been cut through an organ such as the spleen, kidney, etc., bits of glass rod can be embedded so as to bring the halves together evenly.

NORMAL PROPYL ALCOHOL AS A COMBINED DEHYDRATING AND CLEARING AGENT. W. F. SHERIDAN, Army Medical Museum, Washington.

Experiments with normal propyl alcohol have proved its value as a combined dehydrating and clearing agent. Fixed tissue placed in normal propyl alcohol over night has been infiltrated successfully with paraffin the following day. There is an absence of shrinkage and hardening of tissue. There is a remarkable development and preservation of the tissue colors. Fibroid uteri, skin and other areas in which tissues of different density adjoin, and the connective tissue tumors and others undergoing sclerosis, scirrhus carcinomas, which ordinarily are difficult to infiltrate and section with the microtome, are less troublesome when treated with this reagent. Apparent inability to remove water by anhydrous salts, after repeated use, and the high cost, appear to be obstacles to its extensive use.

A MODIFICATION OF ACHUCARRO'S METHOD OF STAINING NEUROGLIA. HELEN INGLEBY, Philadelphia.

The method is the outcome of trials to find the most effective way of demonstrating the course of the fine fibrils of the podics (perivascular feet) of fibrous neuroglia (fibrous astrocytes of Cajal).

(1) Fix in Cajal's formol-bromide using thin slices of fresh tissue not more than 6 hours old. White matter of hemispheres requires from two to four days, spinal cord from seven to ten days. (2) Rinse blocks in distilled water and cut by freezing sections about 15 microns thick. (3) Wash in distilled water quickly and pass them singly into 10 per cent tannic acid (made with distilled water). (4) Warm for from five to seven minutes at 50 C. Allow to cool from ten to thirty minutes. (5) Pass sections into distilled water to which a few drops of ammonia have been added, then wash

in water. (6) Then place in a silver bath made according to Da Fanno's modification of Bielschowsky's method. When sections are yellowish brown, wash rapidly and transfer to (7) 20 per cent formalin which need not be neutral. Reduction is almost instantaneous, the color becoming dark brown. Wash in two changes of distilled water, toned in gold chloride, 1 in 500, fix in 5 per cent hyposulphite of soda; wash, transfer to 50 per cent alcohol, mount on slide, dehydrate and clear in clove or origanum oil, then xylol balsam.

The method is not entirely specific for neuroglia since perivascular connective tissue also stains, but it gives a remarkably clear picture of the perivascular podic processes.

TWO CASES OF A PECULIAR PERFORATION OF THE INTESTINE. ERNEST SCOTT and ROBERT A. MOORE, Ohio State University.

A boy, aged 16 years, dying of lymphoma with severe anemia, was found to have the following condition: complete perforation through the intestinal wall at the duodenofujenal flexure, a portion of the greater omentum passing through the opening like a thread through a needle. The perforation was completely sealed; there was no obstruction of the lumen and no peritoneal adhesions.

Another boy, aged 14 years, died following symptoms of acute high intestinal obstruction. Postmortem examination showed several loops of jejunum and ileum bound together, with the omentum passing through two perforations in the mesentery and three in the intestinal wall. No acute or chronic inflammatory reaction was found about the perforations. No embryologic explanation of the anomaly is offered.

AMEBIC ABSCESS OF LIVER WITH RUPTURE INTO INFERIOR VENA CAVA. R. A. GRISWOLD and STUART GRAVES, Louisville.

A white man, aged 22 years, had symptoms of acute cholecystitis with jaundice, chills, fever and swelling of the feet. He had secondary anemia and hypoleukocytosis. Operation revealed a large amebic abscess of the right lobe of the liver. This was evacuated, but the patient died three weeks later. At necropsy, the liver abscess was found to communicate with the lumen of the inferior vena cava by a ragged opening 1 cm. wide. A mural thrombus partially filled the vein to a point 3 cm. above the bifurcation.

A CASE OF METASTATIC THYROID TUMOR. L. J. RHEA, Montreal.

Mrs. M., aged 60, had had typhoid fever at 16 years. Thyroidectomy was performed five years before the present admission (in 1920). Diagnosis: Hyperplastic adenomatous goiter. In April, 1925, she was admitted with a pathologic fracture of the right femur; it was treated with extension and fixation. On Oct. 10, 1925, the patient had gained weight and the general condition had improved. Exploratory operation showed pulsating fluctuating tumor about the great trochanter. Diagnosis: Aneurysm. Ligation of the internal iliac artery was performed; a plaster cast was used. In February, 1926, after four months in a plaster cast, repeated roentgen-ray treatments showed no healing of the pathologic fracture, and extension of bone destruction. The tumor was larger, visibly pulsating and eroding bone. There was disarticulation at the hip joint, with previous ligation of the common iliac.

Pathologic diagnosis: Metastatic malignant thyroid tumor.

PARINAUD'S CONJUNCTIVITIS. HANFORD MCKEE, Montreal.

This is a form of inflammation of the conjunctiva, first described by Parinaud in 1889. The chief clinical characteristic is that it is always accompanied by inflammation and suppuration in the neighboring lymphatic glands.

Section shows thickening of the epithelium, with the finger-like processes extending into the submucosa, also a wide band of cellular infiltration sharply marked, in the subepithelial tissue. There is an active infiltration of the epithelium with inflammatory cells, mostly polymorphonuclears. In places the epithelium has been replaced by these cells, resulting in microscopic ulceration. In the zone of infiltration numerous thin walled newly formed capillaries are seen, in the lumen of which are polymorphonuclears and lymphocytes. The deep tissue shows practically no change.

A NEW METHOD OF LABELING MUSEUM SPECIMENS. EARL IRISH, L. R. LUNDQUIST and H. E. ROBERTSON, Rochester, Minn.

The method consists in photographing a printed legend and using the film for the label. A yellow background is preferred, and the film can be so stained or can be painted with aluminum or bronze paint. Labeling special features can be accomplished by cutting the film any shape desired.

TECHNIC OF MOUNTING SPECIMENS IN A PARTIAL VACUUM WITHOUT FLUID. L. R. LUNDQUIST and H. E. ROBERTSON, Rochester, Minn.

The method of dry mounting museum specimens or with only a minimal volume of fluid has a number of advantages over mounting in liquid. An apparatus is described which permits drawing a vacuum in a museum container, similar to that used in injection work, only that it is connected with a vacuum line instead of a pressure line.

CRYSTAL VIOLET WEIGERT ELASTIC FIBER STAIN. W. F. SHERIDAN, Army Medical Museum, Washington.

Crystal violet offers the best substitute for basic fuchsin in the preparation of Weigert's elastic tissue stain. The stain is prepared as follows: crystal violet, 1; resorcin, 2; distilled water, 100. This is dissolved by boiling, adding to the boiling mixture 30 cc. of 30 per cent ferric chloride. Boiling is continued until precipitation ceases. The precipitate is collected and, without washing, is dissolved by boiling in 100 cc. of 95 per cent alcohol. This is cooled and filtered and 2 cc. of hydrochloric acid added. The paraffin sections are stained from ten to sixty minutes and differentiated in 95 per cent alcohol until elastic fibers are alone stained, a light green or greenish black.

THE USE OF LOW MELTING POINT PARAFFIN TO PREVENT HARDENING OF TISSUE. W. F. SHERIDAN, Army Medical Museum, Washington.

High melting point paraffin (52 C.) which requires a temperature of from 53 to 54 C. during infiltration often causes a serious shrinking and hardening of tissue; particularly fibroid uteri, skin and other areas where tissues of different density adjoin and in the connective tissue tumors and others undergoing sclerosis. Pieces of tissue that were comparatively soft on palpation before being placed in high melting paraffin were at the end of an hour hard and brittle. This trouble has been almost entirely overcome by first using a low melting point paraffin (40 or 43 C.) in a temperature of 44 C. or less.

After completing the period of infiltration in low melting point paraffin, the pieces of tissue are transferred to high melting point paraffin for a minute or two and embedded.

METHYLENE AZURE B IN STAINING SECTIONS OF HEMATOPOIETIC TISSUES. W. J. MACNEAL and SADA O OTANI, New York.

Methylene azure B (trimethyl thionin), when used in combination with phloxine or eosin following Zenker's or Helly's fixation, gives an extremely crisp differentiation of the protoplasmic granules and hemoglobin content in cells of spleen and bone marrow. It is particularly serviceable demonstrating neutrophilic granules. The detailed method is described. Bensley's technic for granules in pancreatic islets, using azure B, gives even better results.

NOTE ON THE MORPHOLOGY OF THE RENAL EPITHELIA. VERA B. DOLGOPOL, Odessa, Russia.

In an investigation of the finer structure of the kidney using Carnoy-van Gehuchten fixation and Heidenhain's iron-hematoxylin stain, it was found that: 1. The nuclei of the renal epithelia in the mouse and the rabbit shows a distinct nuclear membrane. The chromatin is distributed mostly at the periphery of the cell. The area around the nucleolus is relatively free from chromatin. 2. In places the "rods" are massed together; in others they are scarce, leaving narrow, clear spaces. 3. The cell border may be demonstrated not only by silver precipitation methods, but also by the iron-hematoxylin of Heidenhain. It may be seen in proximity to the clear spaces between the "rods." 4. Occasionally in the mouse, more often in the rabbit, the lining epithelium of Bowman's capsule contains rodlike bodies.

INTERVENTRICULAR SEPTUM DEFECT WITH BRAIN ABSCESS: REPORT OF A CASE.

E. A. BAUMGARTNER and HUBERT SCHOONMAKER, Clifton Springs, N. Y.

A case of ventricular septal defect with normal pulmonic valve and conus is described. Cyanosis and a harsh systolic murmur in the pulmonic area were present, but no thrill. The roentgenogram showed moderate right-sided hypertrophy, the electrocardiogram right preponderance and partial heart block. There was a terminal cerebral abscess from which *Streptococcus hemolyticus* was isolated. No endocarditis or other source of infection was found.

ECONOMICAL PHOTOGRAPHY IN THE LABORATORY. W. R. JAFFREY, Hamilton, Canada.

The author treats of the possibilities which the pathologist has of making good records with very simple equipment and little expense. The requirements are a camera with a good anastigmat lens of about 6½ inch focal length, a box permitting extension up to 13 inches and a reversible back. Cut film has advantages over glass plate and is recommended. Satinet makes a good background for specimens unless they are placed under water. Daylight is preferred to electric light. The same camera can be used for photomicrography with special color filters to suit the requirements. Plates, film and paper should be protected against the roentgen ray and radium, as they may be fogged 6 feet away, even though the radium is in a lead container.

ADIPOSUS DOLOROSA. N. C. FOOT, Cincinnati, Ohio.

The syndrome is: (1) localized accumulation of tenier fat, (2) marked asthenia, (3) psychoses and epileptiform seizures, (4) bullae or ulcers on extremities, (5) subnormal temperature and low metabolic rate. The ductless glands always show pathologic changes; most constant in suprarenals and thyroid, findings in the pituitary are more diversified. Changes in the pancreas and gonads are rather variable. This condition is more prevalent in females.

Report of Case.—A negress, weighing 350 pounds (158.8 Kg.), aged 60, had a history of asthenia and had been fat all her life. There was no history of pain. She had ulcers on her legs. She was comatose, with epileptiform seizures after admission to the hospital. The physical examination was negative owing to her fatness. She died twenty-four hours after admission. The urine showed much albumin and blood. The temperature was 97 F. Necropsy showed adenoma of the hypophysis, adenomas of the suprarenals, an atrophic ovary, persistent thymic tissue and sclerotic pancreas. The kidneys showed chronic glomerulonephritis and vascular nephritis. There were exostoses in the skull, with marked cerebral atrophy localized near the exostoses. Dercum ascribed the disease to thyroid changes, Cushing to pituitary changes; none has called attention to the prevalence of suprarenal adenoma, although this is mentioned. The tumors in our case could hardly be considered the etiologic factor—it was too small, too rapidly-growing and too long-standing.

CARDIAC ANOMALY. A. C. P. HOWARD, Montreal.

Pulmonary stenosis of the conus of the right ventricle, with fusion and stenosis of the pulmonary cusps, and hypoplasia of the pulmonary artery were present; also a large defect of the interventricular septum just anterior to the undefended space; dextroposition of the aorta with dilatation of the ascending arch and hypoplasia of the aortic trunk; inflammatory fusion of aortic cusps, with recent bacterial endocarditis; small patent foramen ovale; tricuspid insufficiency with anomalous insertion of chordae; anomalous network in right auricle; multiple accessory right coronary arteries; dilatation, with slight hypertrophy, of right auricle; marked simple hypertrophy of right ventricle; hypertrophy and dilatation of left ventricle.

The patient was a man, aged 23, presenting a marked congenital cyanosis with extreme clubbing of the fingers and toes and polycythemia; symmetrical enlargement of the thyroid and moderate enlargement of the lymph glands. The spleen was enlarged but not tender. The patient suffered from epileptiform attacks accompanied by unconsciousness, and from hemoptysis; also a suppurative otitis media and bacterial endocarditis. The blood pressure was 180 systolic and 140 diastolic. On examination of the heart, there was a definite systolic thrill over the mitral area with a loud systolic murmur having its maximum intensity over the base. Points of interest were the coexistence of a bicuspid valve above the septal defect which was the seat of a bacterial endocarditis, the marked clubbing (which is characteristic of pulmonary stenosis with ventricular septal defect), and the epileptiform seizures, which are also characteristic of this type of congenital cyanosis when the patient reaches adult life.

"INFARCTION OF THE HEART." V. C. JACOBSON, Albany, N. Y.

The typical clinical syndrome of infarction of the heart consists of: (1) sudden anginal pain in precordium epigastrium; (2) circulatory collapse with acute fall in blood pressure; (3) transient pericardial friction rub; (4) leuko-

cytosis; (5) slight fever. The condition occurs chiefly in elderly, well-nourished and high living persons. Death is often sudden, and varying degrees of pulmonary edema can usually be detected if death is delayed.

There were five typical cases of cardiac infarction, all in men from 54 to 86 years of age. The lower one half to two thirds of the left ventricle wall was involved; the coronary arteries were very sclerotic with most marked disease in the anterior descending branch of the left coronary artery, where a fresh or older thrombus was usually found attached to an atheromatous plaque. This artery was the one responsible for 95 per cent of cardiac infarctions in old people and can rightfully be called "the artery of sudden death in the aged."

COMPLETE TRANSPOSITION OF ARTERIAL TRUNKS WITH STENOSIS OF AORTIC ORIGIN, PATENT DUCTUS BOTALLI, OPEN FORAMEN OVALE AND DEFECT OF INTERVENTRICULAR SEPTUM. M. DREYFUSS, New York.

A mother, aged 35, with signs of mitral insufficiency, gave birth to a second child, which soon developed cyanosis and labored breathing. Clinically it had a large heart, a systolic murmur at the right of the sternum, conveyed to the apex and axilla. Death occurred on the sixth day.

Necropsy showed cyanosis of the thoracic organs and compression of the lungs by the large heart. The aorta arose from the right ventricle anteriorly, the pulmonary artery from the left ventricle to the right and posteriorly—a complete transposition of the arterial trunks; also there were open ductus Botalli and interauricular and interventricular septums.

THE CLINICAL CLASSIFICATION OF CARDIAC DEFECTS. MAUDE E. ABBOTT, Montreal.

There are three definite groups of cardiac anomalies of clinical significance:

1. Cases in which there is no abnormal communication between the two circulations, but the anomaly is the cause of cardiovascular strain or venous stasis, such as bicuspid semilunar valves, coarctation of the aorta, congenital valvular lesions, anomalies of the aortic arch, pericardial degeneration.

2. Cases of arterial venous shunt with transient or terminal reversal of flow, such as defects of patent foramen ovale, interventricular septum, aortic septum or patent ductus arteriosus.

3. Cyanotic group (venous-arterial shunt) of different grades: (a) moderate, pulmonary stenosis with closed septum; dextroposition of aorta with ventricular septal defect; cortiloculare biatriatum; (b) marked pulmonary stenosis with combined defect of interventricular septum and dextroposition of aorta; pulmonary atresia with defect of interventricular septum and dextroposition of aorta; persistent truncus arterionis; (c) extreme coronary biloculare, pulmonary atresia with closed ventricular septum; complete transposition of arterial trunks with closed ventricular septum; mitral and aortic atresia.

ACTIVITIES OF COMMISSION ON STANDARDIZATION OF BIOLOGIC STAINS. R. W. FRENCH, Washington.

Originally organized under the auspices of the National Research Council in 1921 and later reorganized independently, the Commission on Standardization of Biological Stains has carried on a cooperative and scientific study of dyestuffs for biologic stain work since that time. All of the more commonly employed stains have been investigated, and the following certified dyes are obtainable from dealers: anilin blue, water soluble; Bismarck brown Y, brilliant crsyl blue, carmin, congo red, cresyl violet, crystal violet, eosin, yellowish

fuchsin basic, fuchsin acid, gentian violet, indigo carmin, janus green B, light green SF, yellowish methyl green, methyl orange, methylene azure, methylene blue, neutral red, orange G, pyronin, safranin O, sudan III, sudan IV, tetra-chrome stain (MacNeal), thionin, toluidin blue, and Wright's stain.

In 1925, a book on "Biological Stains" was published by the commission, while during the current year the publication of a quarterly journal devoted to stain problems was undertaken. The first issue of *Stain Technology* appeared in January, 1926.

Work under way at this time includes a further investigation of the fat stains, with both the sudan types and Nile blue sulphate as a differential stain. It also is suggested that a type collection of stained slides be formed as an aid in the comparison of technical results. This latter is due to the fact that marked variations in technic are noted, which in many instances account for otherwise supposed variations in dyestuffs. It is proposed that such a type collection may be housed with the Army Medical Museum, Washington, and be available on circulation.

UNIQUE HEART ANOMALY: FREE FIBROUS CORD PASSING THROUGH THREE HEART CHAMBERS TO THE AORTA. E. B. KRUMBHAAR and J. L. GOFORTH, Philadelphia.

A white woman, aged 23, came to necropsy with a clinical diagnosis of postpuerperal psychosis. There had been gallop rhythm, tachycardia and a sound at the apex like a cross between a murmur and friction rub.

The heart weighed 300 Gm.; there was slight right-sided dilatation. The valves and coronary arteries were normal. Arising from the right auricular wall 1.5 cm. from the annulus ovalis a grayish-white, glistening cord 0.5 mm. in diameter passed through the interauricular wall, traversed the left auricle following the blood flow through the mitral valve into the left ventricle, then turned toward the aortic valve, piercing the anterior cusp and attaching itself to the aorta 8 mm. beyond. The cord varied in thickness from 6 mm. to 2 mm., the entire length being 12 cm. Histologically it was made up of collagenous tissue covered with flattened endothelial cells. No explanation of the condition is offered, but it seems to be a developmental anomaly.

A MICROCHEMICAL HISTOLOGIC METHOD FOR DIFFERENTIATION OF TISSUES BY MEANS OF FERRIC SALTS. ERWIN CHRISTELLER and KARL KAISER, Berlin, Germany.

Ferric salts are successful in demonstrating the presence of acids (including lactic acid) in tissues.

Small slices of fresh tissue are put in ferric chloride or other iron salt with formol, and after twenty-four hours frozen sections are made, washed in distilled water, then treated with potassium ferrocyanide and hydrochloric acid. The connective tissues are pale, the nuclei weak blue, the red cells pale green, plasma light green, epithelial cells, dark blue cytoplasm, carcinoma of deeper blue, muscle bright blue. Counter stain may be used, eosin, van Gieson, orange G, alum carmin or phenosafranin. The ferric salts which precipitate in vitro the proteins of the blood give the best picture.

Book Reviews

FORENSIC MEDICINE. A TEXTBOOK FOR STUDENTS AND PRACTITIONERS. By SIDNEY SMITH, M.D. (EDIN.) D.P.H., Principal Medico-Legal Expert, Egyptian Government Service; Professor of Forensic Medicine in the Royal Schools of Medicine and Law, Cairo. With an Introduction by Professor Harvey Littlejohn, F.R.C.S. (Edin.), F.R.S.E., Professor of Forensic Medicine, University of Edinburgh. Price, 21 shillings net. Pp. 498, with 117 illustrations. London: J. & A. Churchill.

In order to meet the needs of medical students and practitioners for a concise manual of forensic medicine, Professor Smith ventures singlehanded to cover practically all parts of that large and complex subject. The early chapters deal with questions of legal procedure, signs of death and later changes, sudden natural death, postmortem examination and identification. These matters are presented in a simple but thorough and practical manner. Special attention is given problems of identification. Undoubtedly many pathologists will not agree that fatty degeneration of the heart muscle is the most common cause of sudden death; and the correctness of classing hemorrhage into the brain as a common cause of sudden death also is open to question unless "sudden" is interpreted to mean in a day or two. Next come chapters in which are discussed wounds and injuries to various parts of the body, deaths from asphyxia of different kinds and examination of blood stains. The illustrations in these and other chapters, all in black and white, are original, always instructive and sometimes unusual and striking. In connection with ruptures and tears of internal organs, a word of warning not to mistake the undertaker's punctures for vital lesions might have been added with advantage, at least for American students. Undertaker's punctures of the heart are known to have been taken as examples of spontaneous rupture. On page 168, in writing of iso-agglutinative blood grouping, the names of Landsteiner, Hirschfeld and Ottenberg are all misspelled. The chapter on wounds from firearms will be found of special value in medicolegal examinations. Chapters 15 to 19 deal with rape, abortion, infanticide and allied topics; then follow a chapter on ethics and law in the conduct of medical practice, and one on insanity and malingering; chapters 22 to 27 take up the general aspects of poisons and poisoning (only one illustration), but systematic chemical toxicology is relegated to the appendix. There is an interesting appendix also on forensic medicine in the East, with special reference to Egypt.

The book is a valuable addition to the literature of forensic medicine. It will be of value in medicolegal work everywhere, and may be recommended as especially suitable for the use of students. The writing is clear, effective and easy to read. The author speaks with the authority of experience and special study. After serving his medicolegal apprenticeship in Edinburgh as assistant to Professor Littlejohn, who writes the introduction, he took the position of chief medicolegal expert in the government service in Egypt and of professor of forensic medicine in the University of Cairo. In investigating the varied medicolegal problems of Cairo, where East meets West, he fortunately has had the advantage of a well-equipped medicolegal institute—an essential provision for satisfactory practical efficiency and progress in forensic medicine. How long will it be before properly organized medicolegal institutes now needed with increasing urgency will come into being in the United States?

MEMORANDA OF TOXICOLOGY. By MAX TRUMPER, B.S., A.M., Formerly Lecturer on Toxicology, Jefferson Medical College, Philadelphia. With Introduction and Addenda by HENRY LEFFMANN, A.M., M.D., Emeritus Pathologic Chemist, Jefferson Hospital, Philadelphia. Cloth. Price, \$1.50. Pp. 230. Philadelphia: P. Blakiston's Son & Co., 1925.

This little book by Trumper is a revision of Tanner's "Memoranda of Poisons," which has served a useful purpose in times past. The book is arranged in four parts: general toxicology and corrosives; simple irritants; specific irritant poisons; neurotic poisons. An appendix on bites and stings has been added and also several addenda by Henry Leffmann on toxicologic subjects. The work is brought up to date by inclusion of such subjects as the hazard of tetra-ethyl lead, the war gases, and mention of possible poisoning from soluble barium salts contaminating, or substituted for, barium sulphate in roentgen-ray work. In the discussion of lead poisoning, no mention is made of the basic stippling of the red blood cells, and little mention is accorded to the importance of examining the feces for lead, both points being given much stress in the report of the committee on the hazards of tetra-ethyl lead. The subject matter is presented clearly and concisely, and includes most of the poisons with which the physician comes in contact. Little attention is given to toxicologic methods and tests, as it is assumed that such work will be done by experts, for whom the book is not intended. The book may be recommended to students and practitioners who may wish to have, in a brief and adequate form for ready reference, a summary of the symptomatology and treatment of the various forms of poisoning.